Geographic Disparities in Liver Allocation and Distribution in the United States: Where Are We Now?

Mario Spaggiari*, Obi Okoye, Kiara Tulla, Pierpaolo Di Cocco, Jorge Almario, E. Benedetti, and Ivo Tzvetanov

Division of Transplantation, Department of General Surgery, University of Illinois at Chicago, Chicago, Illinois

ABSTRACT

Background. Equitable deceased donor liver allocation and distribution has remained a heated topic in transplant medicine. Despite the establishment of numerous policies, mixed reports regarding organ allocation persist.

Methods. Patient data was obtained from the United Network for Organ Sharing liver transplant database between January 2016 and September 2017. A total of 20,190 patients were included in the analysis. Of this number, 8790 transplanted patients had a median Model for End-Stage Liver Disease (MELD) score of 25 (17-33), after a wait time of 129 (32-273) days. Patients were grouped into low MELD and high MELD regions using a score 25 as the cutoff.

Results. Significant differences were noted between low and high MELD regions in ethnicity (white 77.4% vs 60.4%, Hispanic 8.1% vs 24.5%; $P < .001$) and highest level of education (grade school 4.8% vs 8.5%, Associate/Bachelor's degree 19% vs 15.7%, $P < .001$), respectively. Patients in high MELD regions were more likely to be multiply listed if they had a diagnosis of hepatocellular carcinoma (12.1% vs 15%, $P = .046$). Wait-list mortality (4.8% vs 6%, $P < .001$) and wait-list time (110 [27-238] vs 156 [42-309] days, $P < .001$) were greater in the high MELD regions.

Conclusions. These results highlight some of the existing disparities in the recently updated allocation and distribution policy of deceased donor livers. Our findings are consistent with previous work and support the liver distribution policy revision.

THE distribution of deceased donor livers remains a source of heated debate in the transplant community. The Final Rule from the US Department of Health and Human Services in March 2000 was developed out of concern for large geographic disparities in allocation of organs [1]. The rule called for objective and standardized criteria to be used in prospective recipient assessment, and subsequent organ allocation. This led to the development of the Model for End-Stage Liver Disease (MELD) score, and subsequent regional/national sharing policies for allocation of deceased donor livers [2]. The management of patients with hepatocellular carcinoma (HCC) within Milan criteria [3] has also been a subject of discussion. Patients with HCC MELD exception points have been found to have significantly lower dropout rates than matched non-HCC patients [4]. Despite several updates to the organ allocation policies, reports of geographic disparities persist. The etiology of this persistent disparity appears to be multifactorial. A portion of this is due to poorly structured policies [5,6], while transplant center [7] and patient behavior [8–10] have been implicated as other possible factors.

The first 2 authors contributed equally to this work.

This work was supported in part by Health Resources and Services Administration contract 234-2005-37011C. The content is the responsibility of the authors alone and does not necessarily reflect the views or policies of the Department of Health and Human Services, nor does mention of trade names, commercial products, or organizations imply endorsement by the US Government.

*Address correspondence to Dr Mario Spaggiari, MD, Division of Transplantation, Department of General Surgery, University of Illinois at Chicago, 840 S Wood St, CSB 402, Chicago, IL 60612. Tel: (312) 413-3379; Fax: (312) 413-7961. E-mail: mspaggia@uic.edu

0041-1345/19
https://doi.org/10.1016/j.transproceed.2019.07.018

The most recent update is the introduction of the MELD Sodium score, implemented in January 2016 following recognition of the role of hyponatremia as an independent predictor of mortality in cirrhotic patients. This tool allows for proper risk stratification, and subsequent allocation of organs to the sickest patients. Nevertheless, reports of geographic disparity continue to trickle in [11,12]. There have been calls for restructuring the current allocation system [13–17] in favor of a system that truly prioritizes the "sickest-first" approach over proximity.

Since the introduction of the MELD Sodium score, there have been no studies assessing its impact on the reported geographic disparities. This study aims to provide a contemporary evaluation of the deceased donor liver allocation system.

MATERIALS AND METHODS

This study is based on the Standard Transplant Analysis and Research files prepared by the United Network for Organ Sharing (UNOS), containing transplant and registration data for patients until September 30, 2017. The study was exempt from institutional review board approval as it was based on an already existing dataset of deidentified information. Data was obtained by querying the liver transplant and waiting list files. Patient selection was limited to the most recent change in liver allocation rules, which came into effect on January 1, 2016.

Demographic data such as candidate age, sex, ethnicity, and highest educational achievement were obtained. Diagnosis at the time of listing, time spent on the waiting list, death while on the waiting list, laboratory-based MELD Sodium scores at listing, as well as at removal from the waiting list were also collected. Patients with missing MELD scores at listing, or removal, MELD scores < 6, or > 45 were excluded as this data was considered unreliable. Patients receiving living donor organs, or requiring emergent re-transplant following initial transplant failure were excluded.

Transplant specific information such as region of transplant, organ cold ischemia time, distance of organ to transplant center, and organ sharing rule applied were also obtained. Descriptive statistics were obtained for the MELD scores at the time of transplant in each region. Regions were classified as either low MELD, or high MELD depending on the numerical relationship of the median regional MELD to the median national MELD. Patients listed in multiple centers were identified by querying the waiting list for recurring encrypted patient identifiers. Available donor information was used to calculate the donor risk index for transplanted organs using the formula derived by Feng et al [18].

Categorical variables were described as proportions of the denominator population and reported as percentage while continuous variables were reported as median and interquartile range. Certain continuous variables were grouped for analysis using clinically relevant cut-points eg MELD score < 30; 31-40; and > 40. Normality testing of continuous variables was performed using the Shapiro-Wilk test. Univariate analyses were performed using Pearson's χ^2 for categorical variables, and the Mann-Whitney U test for continuous variables. Pearson's χ^2 with Bonferroni adjustments was used for multiple comparisons of multinomial categorical or ordinal variables. Cox proportional hazards regression modelling was used to explore patient survival. Variables differing at $P \leq .2$ were selected from a univariate analysis and entered into a stepwise Cox regression model. Using backward, and forward selection models, variables differing at $P \leq .1$ were entered into the final model to identify factors associated with survival following deceased donor liver transplant in our population. A P value $< .05$ was considered significant. All statistical analyses were performed using SPSS Statistics for MacIntosh version 25.0 (IBM, Armonk, NY, United States).

Table 1. Patient Demographics

Demographic details	All patients (N = 20,190)
Age, y; median (IQR)	57 (49-63)
Male sex, %	12,722 (63)
Ethnicity	
White	13,962 (69.2%)
African American	1781 (8.8%)
Hispanic	3251 (16.1%)
Asian	854 (4.2%)
Native American/	191 (0.9%)
Native Hawaiian/Pacific Islander	33 (0.2%)
Multiracial	118 (0.6%)
Education	
None	80 (0.4%)
Grade school	1327 (6.6%)
High school	7808 (38.7%)
Attended college/technical school	4640 (23%)
Associate/Bachelor's degree	3490 (17.3%)
Post college graduate degree	1393 (6.9%)
Not applicable (< 5 y)	512 (2.5%)
Unknown	820 (4.1%)
Diagnosis	
HCC	4385 (21.7%)
Transplanted patients	8790 (43.5%)
Time on waiting list (listing to transplant), d; median (IQR)	129 (32-273)
Requiring ventilator or organ support at time of listing	770 (3.8%)
MELD score at listing; median (IQR)	17 (11-25)
MELD score at transplant; median (IQR)	25 (17-33)
MELD score at transplant, excluding HCC patients; median (IQR)	27 (19-34)
Death on wait-list	1091 (5.4%)

HCC, hepatocellular carcinoma; IQR, interquartile range; MELD, Model for End-Stage Liver Disease

RESULTS

The UNOS Standard Transplant Analysis and Research file contained data for 214,390 liver transplant candidates (247,638 waiting list entries). Of this number, 21,449 were listed on or after January 1, 2016. We excluded 1259 patients for various reasons: negative MELD score at transplant (n = 175), MELD score between 0 and 6 (n = 67), or > 45 (n = 596), and living donor recipients (n = 421), leaving 20,190 patients for analysis. The final working population includes patients listed from January 1, 2016 through September 30, 2017.

Description of Population

The median age was 57 (49-63) years, with a slight male preponderance (63%). With regards to ethnic distribution, 69.2% were white, 16.1% Hispanic, and 8.8% were African American. The majority of patients had only a high school education

Table 2. MELD Distribution by UNOS Regions

	All	Region 1	Region 2	Region 3	Region 4	Region 5
	N = 8790	n = 341	n = 1039	n = 1726	n = 796	n = 1129
MELD score at transplant						
< 30	5985 (68.1%)	217 (63.6%)	703 (67.7%)	1278 (74%)	511 (64.2%)	536 (47.5%)
31-40	2285 (26%)	100 (29.3%)	283 (27.2%)	386 (22.4%)	229 (28.8%)	425 (37.6%)
> 40	519 (5.9%)	24 (7%)	53 (5.1%)	62 (3.6%)	56 (7%)	168 (14.9%)
Median score (IQR)	25 (17-33)	26 (16-35)	24 (16-33)	23 (17-31)	26 (17-34)	32 (20-38)
Time on waiting list (days)						
Transplanted; median (IQR)	39 (9-152)	74 (13-233)	36 (8-165)	30.5 (8-112)	37 (8-171)	27 (6-121)
All patients; median (IQR)*	129 (33-273)	179.5 (68-344)	141 (33-275.5)	85 (18-215)	154.5 (38-294)	141 (36-320)
Death on waiting list*	1091 (5.4%)	69 (7%)	166 (6.5%)	101 (3.5%)	105 (4.7%)	210 (6.6%)
	6	7	8	9	10	11
	n = 247	n = 677	n = 537	n = 344	n = 931	n = 1022
MELD score at transplant						
< 30	167 (67.6%)	435 (64.3%)	410 (76.4%)	202 (58.7%)	717 (77%)	809 (79.2%)
31-40	70 (28.3%)	195 (28.8%)	117 (21.8%)	110 (32%)	189 (20.3%)	181 (17.7%)
> 40	10 (4%)	47 (6.9%)	10 (1.9%)	32 (9.3%)	25 (2.7%)	32 (3.1%)
Median (IQR)	25 (14-33)	26 (17-34)	23 (15-30)	27 (16-35)	23 (17-30)	23 (16-29)
Time on waiting list (days)						
Transplanted; median (IQR)	89 (16-245.5)	48 (10-197)	62 (15-201)	34.5 (8-166.5)	40 (10-127.5)	41 (12-136)
All patients; median (IQR)*	169 (53.5-296)	147 (37-283)	154 (51-295)	172 (58.5-339.5)	102 (28-225)	93 (26-210)
Death on waiting list*	18 (3%)	96 (5.7%)	75 (5.7%)	94 (8.1%)	66 (3.7%)	91 (5%)

IQR, interquartile range; MELD, Model for End-stage Liver Disease.
*Data on these rows reflects both transplanted and nontransplanted patients.

(38.7%), while 23% had attended college/technical school, 17.3% had an Associate/Bachelor's degree, and 6.9% had a post college graduate degree. During the study period, 43.5% of patients on the waiting list were transplanted. The median time on the waiting list was 129 (32-273) days, while the MELD at time of transplant at 25 (17-33) (Table 1).

Regional Disparity

The distribution of MELD scores at time of transplant in the different regions is presented in Table 2. Regions 2, 3, 8, 10 and 11 had median MELD scores lower than 25. The death rate on the waiting list was significantly lower in regions 3, 6, and 10. Further analysis was performed using the low MELD and high MELD regional groupings (Table 3, Fig 1). With regards to race/ethnicity, the low MELD regions had a significantly larger white population (77.4% vs 60.4%), and a lower Hispanic population (8.1% vs 24.5%, $P < .001$). There were also more Associate/Bachelor's degree holders in the low MELD group (19% vs 15.7%, $P < .001$). Patients with HCC awarded tumor points (9.4% vs 10.9%, $P < .001$), and other non-HCC exceptions (19.8% vs 23.7%, $P < .001$) were more common in the high MELD population. While there was no difference in the incidence of multiple listing in either group, patients with a diagnosis of HCC in the high MELD population were more likely to be listed at multiple transplant centers (12.1% vs 15%, $P = .046$).

Regional Outcome Disparity

Overall, fewer candidates were removed from the waiting list in the low MELD group (14.6% vs 19.4%, $P < .001$). There were also fewer patients requiring ventilator or organ support at the time of listing (3% vs 4.7%, $P < .001$). Waitlist mortality (4.8% vs 6%, $P < .001$) and dropout due to progression of HCC (4.7% vs 8.3%, $P < .001$) were significantly lower in the low MELD regions (Table 4). Conversely, the proportion of patients transplanted in the low MELD group was significantly higher than in the high MELD group (50.8% vs 35.9%, $P < .001$). The median MELD at transplant in non-HCC patients was lower in the low MELD group (25 [19–32] vs 30 [22–36], $P < .001$). In addition, the median donor risk index was significantly lower in the low MELD group (2.1 [1.8-2.6] vs 2.2 [1.8-2.7], $P < .001$). More organs were transplanted locally in the low MELD regions (62.3% vs 60%, $P < .001$), with a corresponding reduction in the reported cold ischemia times (5.5 [4.3-6.8] vs 6.1 [4.9-7.8] hours, $P < .001$). The crude mortality post-transplant was higher in the low MELD regions (6.9% vs 5.8%, $P = .03$).

Multiple Listing Disparity

During the study period, 2302 patients (11.4%) were listed at multiple institutions. Their demographic details are presented in Table 5. When compared to single-center listing patients, these patients were typically younger (56 [46-62] vs 58 [49-63] years old, $P < .001$), and had higher educational achievements (Associate/Bachelor's degree and post college graduate degrees). There were fewer multiply listed patients with HCC exception points than the single-center listed patients (13.5% vs 22.8%, $P < .001$). On the other hand, patients with non-HCC exceptions were significantly higher in the

Table 3. Demographic Distribution in MELD Regions

Demographic	Low MELD Regions* N = 10353	High MELD Regions* N = 9837	*P*
Age, y; median (IQR)	57 (49-63)	57 (49-63)	.208
Male sex, %	6561 (63.4)	6161 (62.6)	.275
Ethnicity			
White	8018 (77.4%)	5944 (60.4%)	< .001
African American	1177 (11.4%)	604 (6.1%)	
Hispanic	843 (8.1%)	2408 (24.5%)	
Asian	219 (2.1%)	635 (6.5%)	
Native American	43 (0.4%)	148 (1.5%)	
Native Hawaiian/ Pacific Islander	3 (0%)	30 (0.3%)	
Multiracial	50 (0.5%)	68 (0.7%)	
Education			
None	25 (0.2%)	55 (0.6%)	< .001
Grade school	490 (4.8%)	837 (8.5%)	
High school	4071 (39.6%)	3737 (38.2%)	
Attended college/ technical School	2259 (22%)	2381 (24.3%)	
Associate/ Bachelor's degree	1948 (19%)	1542 (15.7%)	
Post college graduate degree	715 (7%)	678 (6.9%)	
Not applicable (< 5 y)	249 (2.4%)	263 (2.7%)	
Unknown	521 (5.1%)	299 (3.1%)	
Diagnosis			
HCC exception points	972 (9.4%)	1074 (10.9%)	< .001
Non-HCC exception points	2050 (19.8%)	2336 (23.7%)	< .001
Multiple listing	1172 (11.3%)	1130 (11.5%)	.709
HCC diagnosis	142/1172 (12.1%)	169/1130 (15%)	.046

HCC, hepatocellular carcinoma; IQR, interquartile range; MELD, Model for End-stage Liver Disease.
*Low-MELD regions: 2, 3, 8, 10, 11; high-MELD regions: 1, 4, 5-7, 9.

multiply listed population (27.8% vs 20.9%, $P < .001$). Multiply listed patients spent less time on the waiting list (29.5 [7-99] vs 41 [9-162]) days, $P < .001$), though there was no difference in the proportion of patients transplanted, or wait-list mortality.

Survival Analysis

A Cox proportional hazards regression analysis was performed including variables differing at $P < .2$ from a univariate analysis, and the MELD region variable to determine the impact on patient survival. In this model, patients transplanted in low MELD regions had a decreased survival (hazard ratio: 1.40 [1.16-1.69]) (Table 6, Fig 2).

DISCUSSION

Despite advances in healthcare, the widening gap between organ demand and supply remains. Organ allocation based on wait times was associated with an unacceptable death rate, and eventually gave rise to a continuous medical urgency approach based initially on the Child-Turcotte-Pugh score [19]. The introduction of the MELD score was welcomed as an objective tool to assign deceased donor organs to the sickest patients [20,21]; however, the logistics of organ preservation, transport, and medical urgency continue to be limiting factors to a seamless implementation of the Final Rule.

The distribution system up until December 2018 followed a local-regional-national algorithm. The local distribution unit is the donation service area (DSA), a geographical area administered by a single organ procurement organization (OPO). There are currently 58 OPOs in the United States, serving a variety of populations ranging from single large metropolitan areas, to covering multiple states [22]. To facilitate organ allocation, the Organ Procurement and Transplantation Network (OPTN) system is divided into 11 regions based on historic organ sharing relationships. Organ allocation first occurs at the DSA level, then organs not used within the DSA are shared, first regionally and then nationally [23]. Organ sharing was initially introduced regionally in 2005 as Regional Share 15, and subsequently expanded in 2013 as the Regional Share 35/National Share 15 rule. In the Regional Share 15 rule, organs were first offered to patients with MELD scores ≥ 15 locally and then regionally before making the organs available to local patients with MELD scores < 15. The policy was successful in increasing the number of transplants in patients with MELD ≥ 15; however, no change was observed in organ sharing outside the DSA [24]. Recognition of the high mortality rate in patients with MELD > 35 [25] soon gave way to the Share 35 rule. In this rule, organs are initially offered regionally to candidates with MELD ≥ 35, before local candidates with MELD > 15 but < 35 are considered. Offers are then extended nationally to candidates with MELD ≥ 15, before local candidates with MELD < 15 [2].

It is important to note that the OPTN regional structure was not optimized for organ distribution, a situation that has resulted in persistent geographic disparity. The persistent variance in MELD scores at the time of transplant across the various DSAs continues to pose challenges for the development and implementation of organ allocation policies. In 2013, Gentry [13] posited that the current regional partitioning did not create areas with similar balance of transplant need and allograft supply and advocated for a broader sharing policy to reduce disparities in liver availability. The knowledge of these regional trends is not restricted to the academic community, as patients have been known to list in multiple centers and thus increase their probability of transplant. In fact, patients with means specifically migrate to low MELD transplant centers to achieve transplant [26]. Studies have shown that these patients with higher income, and private insurance are more likely to be transplanted away from home while less privileged patients die on the transplant list [8,9]. Multiple modifications to the

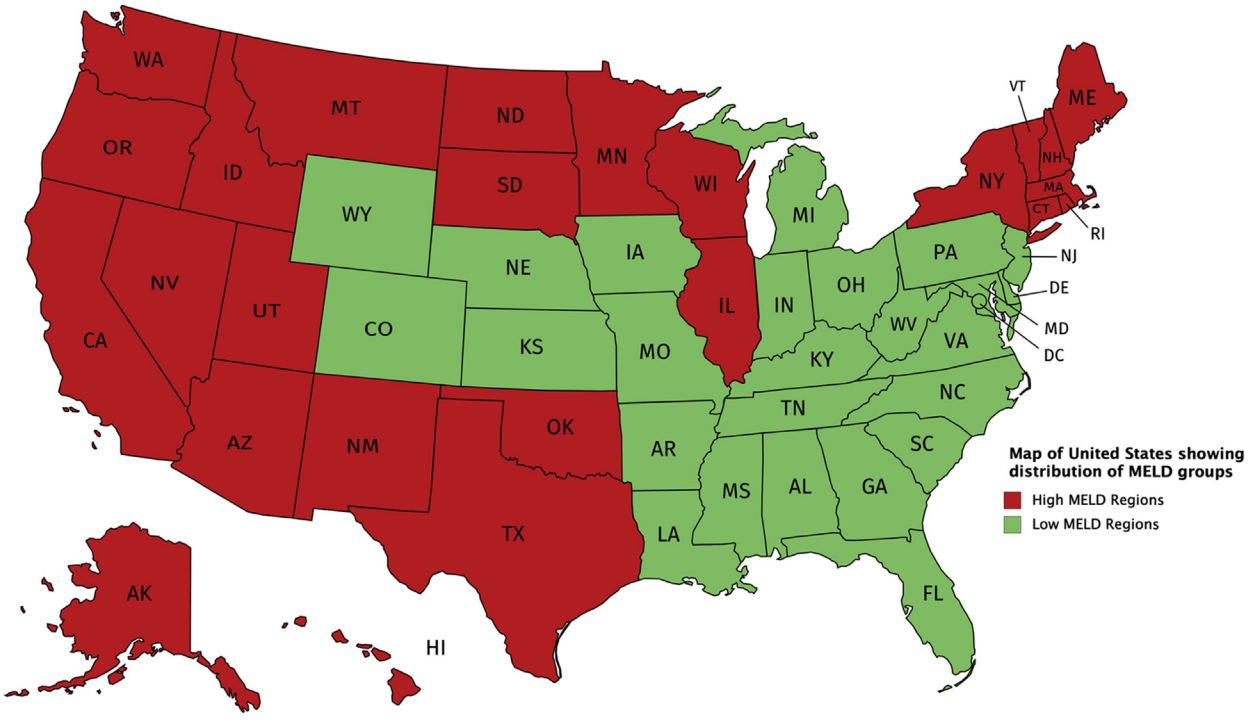

Figure 1. Map of the United States showing the distribution of Meld for End-stage Liver Disease groups

existing structure have been suggested [14–17], and a number of proposals were evaluated by the OPTN. Opposition to the broader sharing policies stems from groups voicing concerns of cost shifting [14], transfer of organs from better-performing centers to poorer-performing centers [27] and increased cold ischemia times from greater distances travelled [28]. It is against this background that the following proposed frameworks were developed by the OPTN: organ distribution (1) based on fixed distance from the donor hospital, (2) on mathematically optimized boundaries, and (3) on continuous distribution without geographic boundaries [29]. A final decision by the Ad Hoc Geography Committee was made in November 2018, following community feedback. The Broader 2 Circle allocation proposal was adopted that, amongst other things, prioritizes liver distribution in the following groups: (1) status 1A and 1B within 500 nautical miles; (2) MELD/PELD at least 29 within 250 nautical miles; (3) MELD/PELD 15-28 within 150 nm, then 250 nm, then 500 nm; and (4) status 1A and 1B and MELD or PELD scores of at least 15 across the nation [30]. This policy change appears to address majority of the concerns raised in this article. Follow-up studies a few years from policy implementation will go a long way to identify any flaws and adjust accordingly.

This analysis of the distribution of deceased donor livers across the country since January 2016 revealed significant geographic and ethnic inequalities. While the differences in the ethnic distribution of the recipients in the different regions may be explained by the resident population in those areas, the geographic disparities in organ allocation require some scrutiny. Our findings, however, remain consistent with findings from prior studies reporting on geographic disparities [13,31]. Patients in regions 2, 3, 8, 10, and 11 had significantly lower MELD scores at listing, and at transplant. In our study population, patients in low MELD regions spent less time on the waiting list, had lower HCC dropout rate, had fewer critically ill patients at the time of listing, and had a lower waiting list mortality. Organs in these regions were predominantly used locally, with fewer organs shared at the national level. A similar regional pattern was investigated in the work by Croome et al [7]. In their study, Croome et al implicated transplant center behavior for some of their findings, suggesting that centers may use marginal organs for their lower MELD recipients after the organ had been declined by multiple other centers. This practice could artificially lower the median MELD score for that center. While this practice may explain some of our findings, the median donor risk index for organs in the lower MELD regions was significantly lower than the high MELD regions. Our findings suggest that other factors other than transplant center behavior are at play. Another factor to consider is the size of the OPOs, and number of transplant centers within the region. In a 2004 study, Trotter found that small OPOs, with fewer than 100 patients on their waiting list were more likely to have fewer patients with

Table 4. Outcomes by MELD Regions

	Low MELD Regions n = 10,353	High MELD Regions n = 9837	P
Removed from waiting list	1507 (14.6%)	1908 (19.4%)	< .001
Too sick to transplant	552 (5.3%)	719 (7.3%)	< .001
Wait-list mortality	499 (4.8%)	592 (6%)	< .001
HCC drop out	312 (4.7%)	435 (8.3%)	< .001
Transplanted patients	5256 (50.8%)	3534 (35.9%)	< .001
MELD at listing	21 (15-28)	24 (15-32)	< .001
MELD at transplant	23 (16-31)	28 (17-36)	< .001
Excluding HCC patients;	25 (19-32)	30 (22-36)	< .001
Time on waiting list (d)			
All listed patients	110 (27-238)	156 (42-309)	< .001
Transplanted patients	38 (9-138)	40 (8-173)	.026
Excluding HCC patients	29 (7-88)	27 (7-100)	.907
Requiring ventilator or organ support	308 (3%)	462 (4.7%)	< .001
Cold ischemia time (h)	5.5 (4.3-6.8)	6.1 (4.9-7.8)	< .001
Sharing practice			
Local	3276 (62.3%)	2120 (60%)	< .001
Regional	1735 (33%)	1146 (32.4%)	
National	245 (4.7%)	268 (7.6%)	
Transplant variables			
Donor risk index	2.1 (1.8-2.6)	2.2 (1.8-2.7)	< .001
Post-transplant mortality	365/5256 (6.9%)	204/3534 (5.8%)	.03

HCC, hepatocellular carcinoma; IQR, interquartile range; MELD, Model for End-stage Liver Disease.

Table 5. Demographics by Listing Pattern

Demographic Details	Multiple Center Listing (n = 2.302)	Single Center Listing (n = 17,888)	P value
Age, y; median (IQR)	56 (44-62)	58 (49-63)	< .001
Male sex, %	1433 (62.3)	11289 (63.1)	.422
Ethnicity			
White	1598 (69.4%)	12364 (69.1%)	.378
African American	222 (9.6%)	1559 (8.7%)	
Hispanic	343 (14.9%)	2908 (16.3%)	
Asian	101 (4.4%)	753 (4.2%)	
Native American	19 (0.8%)	172 (1%)	
Native Hawaiian/ Pacific Islander	6 (0.3%)	27 (0.2%)	
Multiracial	13 (0.6%)	105 (0.6%)	
Education			
None	6 (0.3%)	74 (0.4%)	< .001
Grade school	120 (5.2%)	1207 (6.8%)	
High school	783 (34.2%)	7025 (39.5%)	
Attended college/ technical school	551 (24.1%)	4089 (23%)	
Associate/Bachelor's degree	444 (19.4%)	3046 (17.1%)	
Post college graduate degree	208 (9.1%)	1185 (6.7%)	
Not applicable, < 5 y	74 (3.2%)	438 (2.5%)	
Unknown	103 (4.5%)	717 (4%)	
Diagnosis			
HCC exception points	311 (13.5%)	4074 (22.8%)	< .001
Non-HCC exception points	640 (27.8%)	3736 (20.9%)	< .001
Transplanted patients	1018 (44.2%)	7772 (43.4%)	.489
Time on waiting list (d)	29.5 (7-99)	41 (9-162)	< .001
Requiring ventilator or organ support	198 (8.6%)	572 (3.2%)	< .001
MELD at listing	22 (16-29)	22 (15-30)	< .001
MELD at transplant	25 (16-32)	25 (17-33)	.400
MELD at transplant, excluding HCC	26 (19-33)	27 (20.5-35)	< .001
Wait-list mortality	130 (5.6%)	961 (5.4%)	.593

HCC, hepatocellular carcinoma; IQR, interquartile range; MELD: Model for End-stage Liver Disease.

severe liver disease, with resultant lower MELD transplants [32].

Another interesting finding in our population was the analysis on multiple listing. We found that patients who were multiply listed were younger and had higher educational achievements. We hypothesized that these patients are able to command better paying jobs with more disposable income, in keeping with the previously described stereotypical patient with willingness and means to travel for a liver transplant [8,9]. There was also a higher proportion of patients with HCC in high MELD regions that were multiply listed. This finding in an otherwise relatively healthy population can be explained by the interplay of lower transplant rates and higher transplant MELD scores. Unfortunately, the lack of zip code data made it impossible to identify the primary center and if the transplants occurred at a secondary center. The lower HCC dropout rate in our analysis echoes findings in other studies. Mehta et al reported on regional disparities involving HCC exception patients in long (LWR), medium (MWR), and short (SWR) wait-list regions between 2005 and 2014. They found that patients in SWR (regions 3, 10, 11) had the least dropout compared to MWR (regions 2, 4, 6-8) and LWR (regions 1, 5, 9). There was also a higher percentage of patients in the LWR (41%), and MWR (55%), compared to the SWR (4%) receiving transplants at other centers from their primary listing center [33].

For transplanted patients, there was no difference in crude mortality or graft survival using Kaplan-Meier analysis. After adjusting for covariates, increasing age, MELD score at transplant, donor risk index, hospital length of stay, and transplant in a low MELD region were found to be associated with lower graft survival. Age and recipient MELD have been previously documented to be associated with survival [34,35]. While the other variables are intuitively explained, it remains unclear as to why patients in low MELD regions will have a poorer adjusted outcome.

The study had several limitations, chiefly the retrospective database nature. A number of patients with questionable data

Table 6. Multivariable Cox Regression Analysis for Patient Survival Post-transplant

Factor	n	HR (95% CI)	*P*
Age		1.02 (1.01, 1.02)	< .001
MELD region			
Low MELD	5046	1.40 (1.16, 1.69)	< .001
High MELD	3333	1	
MELD score at transplant		1.02 (1.01, 1.03)	< .001
Donor risk index		1.42 (1.24, 1.62)	< .001
Hospital length of stay post-transplant		1.01 (1.00, 1.01)	< .001
Ventilator/Other life support at time of transplant			
No	7939	1	< .001
Yes	440	1.75 (1.32, 2.34)	
Transplant year			
2016	4038	0.77 (0.64, 0.94)	.011
2017	4341	1	
Non-HCC exclusion indication			
No	7043	1	.035
Yes	1336	1.32 (1.02, 1.70)	

Nonsignificant variables in model: ethnicity, educational status, HCC exclusion indication, time on waiting list.
HCC, hepatocellular carcinoma; HR, hazard ratio; MELD, Model for End-stage Liver Disease.

e.g. negative MELD scores, MELD < 6, or > 45 were excluded. Undoubtedly, some patients with valid data were inadvertently excluded by this approach, including patients with HCC who were listed with awarded MELD points. However, the working dataset derived from this had fewer missing variables, and thus better-quality results. Secondly, specifically identified patients with MELD exception points from HCC, as this is the most common indication for exception. The remaining heterogeneous population of patients make up a relatively small proportion and listing each individual diagnosis in this analysis would make the results difficult to interpret. In addition, various patient comorbidities are not reflected in the MELD score but may contribute to patient outcomes. These factors are not captured in the database, and not accounted for. We were unable to obtain patient zip code information from UNOS, as this variable has been determined to be protected health information. In lieu of this metric (typically used in estimating median household income), we explored the highest academic achievement variable because studies have demonstrated strong links between higher education and higher lifetime earnings [36]. Lastly, the disparities reported in this paper only explore regional differences, which are not representative of the true situation, as it is common knowledge that inequalities exist even at the level of the transplant centers, and the DSA [7].

In conclusion, the deceased donor liver allocation system remains a work in progress. It is anticipated that the revised policy will minimize dropout and deaths from the waiting list. Studies into the post-transplant care of recipients are also warranted to prevent avoidable morbidity.

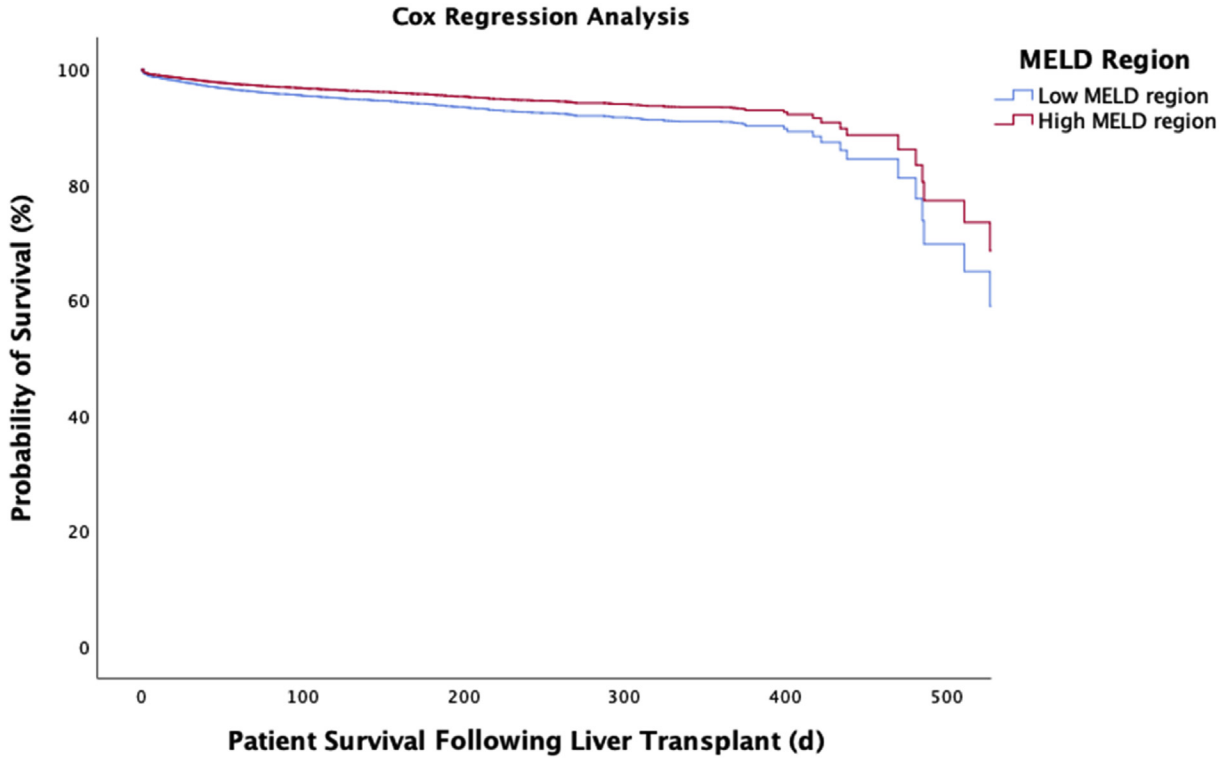

Figure 2. Cox Regression analysis evaluating patient survival following liver transplant in the Meld for End-stage Liver Disease regions

REFERENCES

[1] Institute of Medicine Committee on Organ Procurement and Transplantation Policy. Organ procurement and transplantation: assessing current policies and the potential impact of the DHHS Final Rule. Washington DC: National Academies Press; 1999.

[2] Elwir S, Lake J. Current status of liver allocation in the United States. Gastroenterol Hepatol (NY) 2016;12:166–70.

[3] Mazzaferro V, Bhoori S, Sposito C, Bongini M, Langer M, Miceli R, et al. Milan criteria in liver transplantation for hepatocellular carcinoma: an evidence-based analysis of 15 years of experience. Liver Transpl 2011;17(Suppl. 2):S44–57.

[4] Goldberg D, French B, Abt P, Feng S, Cameron AM. Increasing disparity in waitlist mortality rates with increased model for end-stage liver disease scores for candidates with hepatocellular carcinoma versus candidates without hepatocellular carcinoma. Liver Transpl 2012;18:434–43.

[5] Ladin K, Zhang G, Hanto DW. Geographic disparities in liver availability: accidents of geography, or consequences of poor social policy? Am J Transplant 2017;17:2277–84.

[6] Nadim MK, DiNorcia J, Ji L, Groshen S, Levitsky J, Sung RS, et al. Inequity in organ allocation for patients awaiting liver transplantation: rationale for uncapping the model for end-stage liver disease. J Hepatol 2017;67:517–25.

[7] Croome KP, Lee DD, Burns JM, Keaveny AP, Taner CB. Intraregional model for end-stage liver disease score variation in liver transplantation: disparity in our own backyard. Liver Transpl 2018;24:488–96.

[8] Schwartz A, Schiano T, Kim-Schluger L, Florman S. Geographic disparity: the dilemma of lower socioeconomic status, multiple listing, and death on the liver transplant waiting list. Clin Transplant 2014;28:1075–9.

[9] Vagefi PA, Feng S, Dodge JL, Markmann JF, Roberts JP. Multiple listings as a reflection of geographic disparity in liver transplantation. J Am Coll Surg 2014;219:496–504.

[10] Kadry Z, Schaefer EW, Uemura T, Shah AR, Schreibman I, Riley TR III. Impact of geographic disparity on liver allocation for hepatocellular cancer in the United States. J Hepatol 2012;56:618–25.

[11] Beal EW, Tumin D, Sobotka L, Tobias JD, Hayes D Jr, Pawlik TM, et al. Patients from Appalachia have reduced access to liver transplantation after wait-listing. Prog Transplant 2018;28:305–13.

[12] Monlezun DJ, Darden M, Friedlander P, Balart L, Parker G, Buell JF. Racial and regional disparity in liver transplant allocation. Surgery 2018;163:612–6.

[13] Gentry SE, Massie AB, Cheek SW, Lentine KL, Chow EH, Wickliffe CE, et al. Addressing geographic disparities in liver transplantation through redistricting. Am J Transplant 2013;13:2052–8.

[14] Deshpande R, Hirose R, Mulligan D. Liver allocation and distribution: time for a change. Curr Opin Organ Transplant 2017;22:162–8.

[15] Bittermann T, Goldberg DS. Liver redistricting: what are the upcoming changes in liver allocation in the United States? Curr Opin Organ Transplant 2017;22:112–7.

[16] Axelrod DA, Vagefi PA, Roberts JP. The evolution of organ allocation for liver transplantation: tackling geographic disparity through broader sharing. Ann Surg 2015;262:224–7.

[17] Mehrotra S, Kilambi V, Bui K, Gilroy R, Alexopoulos SP, Goldberg DS, et al. A concentric neighborhood solution to disparity in liver access that contains current UNOS districts. Transplantation 2018;102:255–78.

[18] Feng S, Goodrich NP, Bragg-Gresham JL, Dykstra DM, Punch JD, DebRoy MA, et al. Characteristics associated with liver graft failure: the concept of a donor risk index. Am J Transplant 2006;6:783–90.

[19] Freeman RB, Rohrer RJ, Katz E, Lewis WD, Jenkins R, Cosimi AB, et al. Preliminary results of a liver allocation plan using a continuous medical severity score that de-emphasizes waiting time. Liver Transpl 2001;7:173–8.

[20] Freeman RB Jr, Wiesner RH, Harper A, McDiarmid SV, Lake J, Edwards E, et al. The new liver allocation system: moving toward evidence-based transplantation policy. Liver Transpl 2002;8:851–8.

[21] Kanwal F, Dulai GS, Spiegel BM, Yee HF, Gralnek IM. A comparison of liver transplantation outcomes in the pre- vs. post-MELD eras. Aliment Pharmacol Ther 2005;21:169–77.

[22] OPTN/UNOS Liver and Intestinal Organ Transplantation Committee. Redesigning liver distribution to reduce variation in access to liver transplantation. https://optn.transplant.hrsa.gov/media/1269/liver_concepts_2014.pdf. [Accessed 10 February 2018].

[23] Roberts JP, Dykstra DM, Goodrich NP, Rush SH, Merion RM, Port FK. Geographic differences in event rates by model for end-stage liver disease score. Am J Transplant 2006;6:2470–5.

[24] Pomfret EA, Fryer JP, Sima CS, Lake JR, Merion RM. Liver and intestine transplantation in the United States, 1996-2005. Am J Transplant 2007;7:1376–89.

[25] Sharma P, Schaubel DE, Gong Q, Guidinger M, Merion RM. End-stage liver disease candidates at the highest model for end-stage liver disease scores have higher wait-list mortality than status-1A candidates. Hepatology 2012;55:192–8.

[26] Kohn R, Kratz JR, Markmann JF, Vagefi PA. The migrated liver transplantation candidate: insight into geographic disparities in liver distribution. J Am Coll Surg 2014;218:1113–8.

[27] Gentry SE, Chow EK, Massie A, Luo X, Shteyn E, Pyke J, et al. Liver sharing and organ procurement organization performance under redistricted allocation. Liver Transpl 2015;21:1031–9.

[28] Gentry SE, Chow EK, Wickliffe CE, Massie AB, Leighton T, Segev DL. Impact of broader sharing on the transport time for deceased donor livers. Liver Transpl 2014;20:1237–43.

[29] Organ Procurement and Transplantation Network. Geographic organ distribution principles and models recommendations report. https://optn.transplant.hrsa.gov/media/2506/geography_recommendations_report_201806.pdf. [Accessed 10 February 2018].

[30] Organ Procurement and Transplantation Network, OPTN/UNOS Ad-hoc geography committee minutes November 27, 2018. https://optn.transplant.hrsa.gov/media/2823/20181127_geography_committee_minutes.pdf. [Accessed 31 January 2019].

[31] Yeh H, Smoot E, Schoenfeld DA, Markmann JF. Geographic inequity in access to livers for transplantation. Transplantation 2011;91:479–86.

[32] Trotter JF, Osgood MJ. MELD scores of liver transplant recipients according to size of waiting list: impact of organ allocation and patient outcomes. JAMA 2004;291:1871–4.

[33] Mehta N, Dodge JL, Hirose R, Roberts JP, Yao FY. Increasing liver transplant waitlist dropout for hepatocellular carcinoma with widening geographical disparities: implications for organ allocation. Liver Transpl 2018;24:1346–56.

[34] Roberts MS, Angus DC, Bryce CL, Valenta Z, Weissfeld L. Survival after liver transplantation in the United States: a disease-specific analysis of the UNOS database. Liver Transpl 2004;10:886–97.

[35] Pischke S, Lege MC, von Wulffen M, Galante A, Otto B, Wehmeyer MH, et al. Factors associated with long-term survival after liver transplantation: a retrospective cohort study. World J Hepatol 2017;9:427–35.

[36] Tamborini CR, Kim C, Sakamoto A. Education and lifetime earnings in the United States. Demography 2015;52:1383–407.