ORIGINAL ARTICLE

Geographic Disparities in Deceased Donor Liver Transplantation Within a Single UNOS Region

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Although the Model for End-Stage Liver Disease (MELD) scoring system has improved the ability to measure medical urgency for transplantation, geographic disparities in the probability of being delisted as a result of complications of end-stage liver disease or death and in the probability of orthotopic liver transplantation (OLT) remain. The purpose of the current study was to identify factors associated with these variations among donor service areas (DSAs) in one United Network for Organ Sharing (UNOS) region. Data for 2,948 candidates listed for OLT within 4 DSAs in UNOS region 4 between February 2002 and November 2005 were obtained from UNOS. Multivariate regression models were used to identify study factors associated with delisting (due to deterioration or death) and likelihood of OLT. After risk adjustment for candidate characteristics, those listed in DSA-3 and DSA-4 were at significantly higher risk of delisting than candidates listed in DSA-2 (hazard ratio, 1.22 and 1.10 vs. 0.87 for DSA-2; $P = 0.01$ and 0.05, respectively). In addition, the likelihood of OLT was significantly higher for candidates listed in DSA-1 than in DSA-2, DSA-3 or DSA-4 (hazard ratio, 1.00 compared with 0.45, 0.77, and 0.51; $P < 0.001$ for all pairwise comparisons). Despite the implementation of the MELD system, great geographic disparities exist in the likelihood of delisting and for OLT, suggesting the need for further refinement in regional allocation strategies. ***Liver Transpl 13:747–751, 2007.*** © **2007 AASLD.**

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In the first 20 years after the introduction of orthotopic liver transplantation (OLT), patient survival was dismal, reaching only 20-30% at 1 year.[1,2] During this early phase in liver transplantation, few OLTs were attempted, and the allocation of liver allografts was an informal process performed by clinicians.[3] Refinements in surgical technique and the introduction of more effective immunosuppression has led to dramatic improvement in posttransplantation patient survival.[4] OLT is now offered to many more patients as a treatment for end-stage liver disease. The population of liver transplantation candidates outnumbers the organs available, leading to the complex problem of how to allocate organs to the most deserving recipients.

In 1984, the allocation of organs became a regulated process when the U.S. Congress passed the National Organ Transplant Act.[5] This act created the Organ Procurement and Transplantation Network, a network of regional organ allocation offices that have been supervised by the United Network for Organ Sharing (UNOS) since 1987. Initially, livers were allocated to patients primarily on the basis of time spent on the waiting list. Also, organs were allocated within the geographic area in which they were harvested in order to minimize cold ischemic time.[6] It soon became apparent that this regional allocation system led to some geographic disparities in the probability of liver transplantation once listed. In a focused study of solid organ allograft allocation, the Institute of Medicine noted geographic inequalities in access to organ transplantation and recommended that allograft allocation should be based on medical urgency rather than waiting time or geographic location.[7]

Subsequently, the Department of Health and Human Services revised the section of federal legislation outlining the allocation process, mandating that solid organ

Abbreviations: DSA, donor service area; MELD, Model for End-Stage Liver Disease; OLT, orthotopic liver transplantation; UNOS, United Network for Organ Sharing.

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allograft allocation "[s]hall not be based on the candidate's place of residence or place of listing."[8] In 2002, in response to this mandate, the Model for End-Stage Liver Disease (MELD) scoring system, was implemented, which gave clinicians a method to rank patients on the basis of medical urgency. The MELD score has improved the ability of clinicians to quantify disease severity, but the extent to which geographic disparities continue to affect organ allocation has not been well defined.

In the current study, liver allograft allocation and candidate characteristics in one UNOS region were examined as a case study to determine whether the Institute of Medicine's recommendations regarding both prioritizing patients on the basis of medical urgency and avoiding arbitrary discrepancies that are based on geography have been met.

MATERIALS AND METHODS

All liver transplant candidates ≥18 years of age that were placed on the UNOS liver transplant waiting list in UNOS region 4 (comprised mainly of Texas and Oklahoma) from February 2002 to November 2005 were included in this study. The individual region 4 DSAs have been renamed to prevent identification.

Individual liver transplant candidate data was obtained from the UNOS Organ Procurement and Transplantation Network database. Variables collected included DSA, match MELD score at removal from waiting list, reason for removal from waiting list (delisted for deterioration or death vs. transplantation), status 1 designation, age, race, presence of any MELD exceptions, and double listing status. Multiorgan transplant candidates or recipients were excluded. Unless otherwise indicated, MELD scores reported are match MELD scores (calculated MELD plus any exception points). Double-listed patients (patients listed as candidates at more than one transplant center) were identified as those candidates whose database-specific patient identification number appeared during the same time period in association with 2 different transplant centers.

To determine each DSA's organ procurement performance, the crude donation and crude organ-specific donation rates for each DSA were obtained from the Scientific Registry of Transplant Recipients (SRTR). These rates are based on deceased donors per 100 deaths that met criteria for organ donation. The rates were compared with national averages and with calculated expected rates for each region (as defined by the SRTR).[9]

Continuous study variables were first compared with a 1-way analysis of variance. If they were significant, pairwise comparisons were then performed with the Student *t* test with Bonferroni correction. Categorical variables were compared with χ^2 tests. Likelihood of delisting (due to deterioration or death) and of undergoing OLT was examined by multivariate Cox proportional hazards models. In the model examining hazard of delisting, candidates removed from the waiting list because of transplantation or improvement of medical condition were censored. The models were built by using purposeful selection of covariates as described by Hosmer and Lemeshow.[10] All statistical analyses were performed by SPSS version 11.0 (SPSS, Chicago, IL) and Stata version 8.0 (StataCorp, College Station, TX).

RESULTS

Demographic and Listing Characteristics of Region 4 Liver Transplant Candidates

Together, the 4 DSAs encompassed by region 4 serve approximately 25.3 million people. Rates of organ donation for the 4 DSAs ranged from 52.5 per 100 to 62.9 per 100 deaths that met criteria for organ donation. These rates did not differ much from SRTR calculated expected rates. Liver-specific donation rates ranged from 47.1 per 100 to 56.5 per 100 deaths (the national average is 53.1 per 100). Again, there was no marked variation from the expected number of liver donors. It should be noted that the geographic areas covered by the DSAs in region 4 are noncontiguous.

During the course of the study period (February 2002 to November 2005), 2,948 adult candidates were listed for liver transplantation a total of 3,252 times within region 4. This represented approximately 9.6% of the total candidates listed in the United States during this time period. The median age of these patients was 52 years (range, 18-80 years). More patients were male (1,740 candidates, or 59.0%) than female (1,208 candidates, or 41.0%). Most candidates were white (n = 1,858, or 63.0%), followed by Hispanic (n = 788, or 26.7%), African American (n = 211, or 7.2%), and Asian (n = 61, or 2.1%). The remaining 30 candidates (1%) were described as either multiethnic or of unknown ethnicity. Sixty-two candidates (2.1%) had previously undergone liver transplantation. In total, 287 candidates (9.7%) were listed for liver transplantation at 2 or more transplant centers. This represented 22.8% of all the double-listed candidates in the United States during the study period.

Severity of Illness Among Candidates Within Region 4

To evaluate the variability in the severity of illness between geographically different areas, MELD scores of patients in the different DSAs were calculated. Ninety-two (2.8%) of the 3,252 total adult candidate listings within region 4 were designated as status 1 at the time of removal from waiting list. The median MELD score of the non–status 1 candidate listings at the time of removal from waiting list was 18 points (range, 6-40 points). MELD exceptions were given for 463 candidate listings (14.7%); 337 (72.8%) of these were for hepatocellular carcinoma.

MELD scores of non–status 1 candidates that underwent OLT differed among the DSAs within region 4 (overall $P < 0.0001$). The mean MELD score in DSA-1 (20.7) was lower than that of all other DSAs in region 4

TABLE 1. MELD Score of Adult Liver Transplant Candidates at Time of Transplant

DSA	No. of transplants	Mean match MELD score at OLT of non–status 1 candidates
DSA-1	147	20.7*
DSA-2	305	25.8†
DSA-3	477	22.4
DSA-4	424	23.4

Abbreviations: DSA, donor service area; MELD, Model for End-Stage Liver Disease; OLT, orthotopic liver transplantation.
*DSA-1 mean match MELD score was less than that of DSAs 2, 3, and 4 (all pairwise P values < 0.05).
†DSA-2 mean match MELD score was greater than that of DSAs 1, 3, and 4 (all pairwise P values < 0.001).

TABLE 2. Characteristics of Adult Liver Transplant Candidates Delisted Due to Death or Deterioration

DSA	No. of delistings	Mean match MELD score for all patients delisted	Mean match MELD score for non–status 1 patients delisted
DSA-1	28	26.4	26.3
DSA-2	115	26.0	26.0
DSA-3	117	21.2	20.9*
DSA-4	156	26.1	25.5*

Abbreviations: DSA, donor service area; MELD, Model for End-Stage Liver Disease.
*Mean match MELD score for non–status 1 patients delisted in DSA-3 was less than that of patients in DSA-4 with a pairwise P value of 0.004.

($P < 0.05$ for all pairwise comparisons), while the mean MELD score in DSA-2 (25.8) was higher than that of all other DSAs in region 4 ($P < 0.001$ for all pairwise comparisons) (Table 1). The mean MELD scores of DSA-3 and DSA-4 (22.4 and 23.4, respectively) were not different from one another ($P = 0.21$). When factoring in the number of non–status 1 candidates, the mean MELD scores of these candidates delisted because of death or deterioration of medical condition was lower in DSA-3 than in DSA-4 (20.9 vs. 25.5; $P = 0.004$), but otherwise did not differ between DSAs (Table 2).

Delisting (Due to Death or Deterioration)

There were 416 delistings (due to death or deterioration) representing 12.8% of all candidate listings in region 4 during the study period. To determine whether the risk of delisting differed in a statistically significant manner among DSAs in region 4, a multivariate Cox proportional hazards model was created. Increasing laboratory MELD score (hazard ratio [HR] = 1.10, $P < 0.001$), status 1 designation (HR = 8.59, $P < 0.001$), and increasing age (HR = 1.01, $P = 0.01$) were associated with increased risk of delisting. African American candidates had lower delisting rates as compared with non–African American candidates (HR = 0.62, $P = 0.05$). The presence of an active MELD exception and double listing were also associated with reductions in risk of delisting (HR = 0.36, 0.59; $P = 0.003$, 0.002, respectively).

The hazard rate for delisting associated with each of the 4 DSAs within region 4 ranged from 0.87 to 1.22. Pairwise comparison determined that the hazard rate for DSAs 3 and 4 were higher than for DSA-2 ($P = 0.01$, 0.05, respectively). This finding suggests that, after adjusting for relevant candidate characteristics (MELD score, MELD exceptions, and double-listing practices), the risk of delisting for candidates listed in DSA-3 and DSA-4 was higher than the risk of delisting for DSA-2 candidates (Table 3).

Likelihood of Undergoing OLT

To identify factors associated with likelihood of undergoing OLT, a second multivariate proportional hazard model was performed. The results of this analysis demonstrated that after adjusting for age, laboratory MELD score, MELD exceptions, status 1 designation, age, and double-listing, candidates listed in DSA-2, DSA-3, and DSA-4 had a 23-55% lower likelihood of undergoing OLT than candidates listed in DSA-1. Ethnicity was not associated with likelihood of undergoing OLT and was therefore not included in the final model (Table 4).

DISCUSSION

In 1999, the Institute of Medicine studied organ allocation in the United States and published recommendations to make the process more equitable.[7] Among those was the recommendation that liver allografts be distributed to patients in order of decreasing disease severity. It was acknowledged that geographic disparities in access to transplantation existed, and the Institute of Medicine recommended that existing organ procurement organizations should share organs in a larger uniform organ allocation area, each serving at least 9 million people. It was hoped that this would minimize disparities in organ allocation that were based on geographical boundaries. Subsequently, the Department of Health and Human Services revised the Code of Federal Regulations legislating organ procurement and transplantation.[7] This revised legislation mandated that organ allocation be based on an objective scoring system, not on place of residency or place of listing. In February 2002, UNOS adopted the MELD scoring system as an improved means to quantify disease severity and prioritize candidates. Although the adoption of the MELD system satisfied the recommendations of the Institute of Medicine, no formal steps have been taken to address geographic inequalities in access to OLT.

TABLE 3. Results of a Multivariate Cox Proportional Hazards Model of Delisting

Covariate	Hazard ratio	95% confidence interval	*P* value
Laboratory MELD score (by point)	1.10	1.10–1.11	<0.001
Status 1 designation	8.59	4.35–17.00	<0.001
Age (by year)	1.01	1.00–1.03	0.01
Black ethnicity	0.62	0.39–0.99	0.05
Active MELD exception	0.36	0.19–0.71	0.002
Double listed	0.59	0.43–0.83	0.002
DSA			
DSA-1 (reference)	1.00	. . .	. . .
DSA-2	0.87	0.57–1.31	0.50
DSA-3	1.22	0.80–1.86	0.35
DSA-4	1.10	0.73–1.65	0.64

Abbreviations: DSA, donor service area; MELD, Model for End-Stage Liver Disease.

TABLE 4. Results of a Multivariate Cox Proportional Hazards Model of Undergoing Orthotopic Liver Transplantation

Covariate	Hazard ratio	95% confidence interval	*P* value
Laboratory MELD score (by point)	1.07	1.06–1.07	<0.001
Status 1 designation	8.44	6.31–11.29	<0.001
Age (by year)	0.99	0.989–0.999	0.05
Active MELD exception	5.08	4.48–5.77	<0.001
Double listed	0.60	0.50–0.72	<0.001
DSA			
DSA-1 (reference)	1.00	. . .	. . .
DSA-2	0.45	0.36–0.55	<0.001
DSA-3	0.77	0.64–0.93	0.008
DSA-4	0.51	0.42–0.61	<0.001

Abbreviations: DSA, donor service area; MELD, Model for End-Stage Liver Disease.

By use of UNOS region 4′s liver allograft allocation and candidate characteristics as a case study, the results of the current analysis demonstrate that geographic inequalities in organ allocation still exist, even after the implementation of the MELD system. These differences include both the likelihood of delisting and of transplantation once listed. DSA size was closely associated with these outcomes.

Examination of the 4 DSAs reveals that DSA-1 encompasses the smallest population, has the lowest number of waiting list candidates, and tends to assign transplants to patients who are less sick as assessed by the MELD scoring system. This replicates similar findings in previous studies such as that of Trotter and Osgood,[11] who demonstrated that only 19% of OLT recipients in donor service areas (DSAs) with <100 candidates had MELD scores >24, compared with 49% in DSAs with ≥100 candidates. Two possible explanations that they offered for this phenomenon included that fewer numbers of sick patients are listed in small DSAs, and that sicker patients migrate to larger metropolitan areas for health care.[11] In addition, Schaffer et al.[12] reported that despite the introduction of the MELD scoring system, intraregional allocation disparities existed within a single region and recommended that intraregional sharing of deceased liver allografts be adopted.

Considering the practice of double listing candidates, it was hypothesized that these patients would have an unfair advantage over single-listed candidates. However, our data show that although being double listed is associated with a lower risk of deterioration or death while on the waiting list, it does not increase the likelihood of receiving a transplant. A possible explanation is that patients who are double listed may be those who are less sick and therefore have a better chance of survival, but who are not receiving transplants as often. Given that double listing does not appear to increase the likelihood of transplantation, the merits of this practice should be studied further.

After adjusting for MELD score, status 1 designation, and double listing, our analysis also found geographic differences in the risk of delisting. The hazard model showed that patients in DSA-3 and DSA-4 had a far higher risk of delisting. This points to factors that are not accounted for by the MELD score. Similar findings were seen when the hazard model for transplantation was analyzed. After correction for variables, including

MELD score, patients in DSA-2, -3, and -4 had a lower likelihood of receiving a transplant as compared with those in DSA-1.

Some of the disparities seen in this study may have been attributable to differences in practice patterns among the various studied DSAs. For example, removing a patient from the waiting list due to deterioration of medical status requires clinical judgment that is partially subjective and therefore may differ from physician to physician and from DSA to DSA. In addition, allograft offer acceptance rates are determined by multiple subjective assessments of donor and recipient factors. These and other variations in practice patterns may account for the differences observed in our study. Regardless, these disparities are not accounted for by the current MELD system and merit further attention.

This analysis raises the question: "Will increased intraregional sharing decrease the observed geographic inequalities in access to OLT?" Liver transplant centers and UNOS regions have adopted regionwide sharing for UNOS status 1 adults and children, and evidence from 2 different UNOS regions has demonstrated that sharing for status 1 candidates decreases their waiting list mortality.[13,14] More recently, Organ Procurement and Transplantation Network policy has been expanded to mandate sharing of liver allografts if no candidate within the DSA has a MELD score of >15. Whether this policy will decrease waiting list mortality in this subgroup and minimize geographic inequalities in access to OLT remains to be seen.

In summary, our analysis demonstrated that variation in liver allograft allocation exists in region 4. Previous studies have found this to be true in other regions.[11,12] Further research is required to determine whether intraregional organ allocation disparities exist in other regions and to elucidate specific factors that affect likelihood of liver transplant candidates receiving organs that are not accounted for by the current MELD system. In the interim, increased intraregional sharing of liver allografts in areas with geographic disparities may make the process more equitable for all candidates.

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