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Offer Patterns of Nationally Placed Livers by Donation Service Area

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We previously reported that national liver distribution is highly concentrated in 6 US centers, and this raises the possibility of expedited placement. Therefore, we evaluated all national offers of nationally placed livers (n = 1625) to adult wait-list candidates from February 2005 to January 2010. We developed a model to predict national utilization pathways; pathways exceeding the best-fit linear unbiased predictions by ≥3 standard errors were defined as preferred. All 51 donation service areas (DSAs) placed 1 or more livers nationally, but the percentage per DSA ranged from 1% to 36%. Of 2830 possible national DSA-center pathways, 87% were used. Five hundred eighty livers (36%) were accepted on the first national offer. Four DSAs accounted for 47% of first-national-offer livers, and 44% of these were accepted by a single center. In comparison with first-offer livers using nonpreferred pathways, first offers along a preferred pathway were offered to fewer status 1 candidates (19% versus 61%) and had lower median Model for End-Stage Liver Disease (MELD) scores (22 versus 36, \( P < 0.001 \)). In conclusion, DSA placement patterns of national livers vary widely, with 4 DSAs exporting a high proportion of national livers on the first national offer to non–status 1 candidates with MELD scores less than their local transplant MELD scores. Although this practice may facilitate liver placement, it raises the possibility of expedience trumping patient need. Here we propose changes to the national liver distribution system that will help to balance equity, efficiency, and transparency.


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Currently, deceased donor livers are primarily allocated and distributed within the donation service area (DSA) in which the donor is located.1 These service areas are governed by organ procurement organizations (OPOs) that coordinate the donation and distribution process once actual donors have been identified. Within the DSAs (there are currently 58), there are transplant centers that place patients on organ-specific wait lists. Each transplant center is a member of a specific DSA.

When a donor liver becomes available, the Organ Procurement and Transplantation Network (OPTN) generates a list of candidates in the order in which the OPO must offer the liver. This match run prioritizes the candidates in accordance with OPTN policy, which considers not only the Model for End-Stage Liver Disease (MELD) score but also the location of the listing transplant center with respect to the donor (ie, local [within the DSA in which the transplant center is located], regional [within 1 of the 11 regions in the United States], or national [outside the United Network for Organ Sharing (UNOS) region]). After offers are made to status 1 patients located within the same region as the donor, the liver is next offered, in MELD...
score order, to candidates within the donor’s DSA governed by the local OPO. If the liver is refused by all local candidates with MELD scores ≥15, it is offered to candidates residing outside the local DSA but within the UNOS region in which the liver was procured and then to candidates outside the UNOS region.

This allocation and distribution algorithm attempts to enhance organ availability for candidates according to disease severity while limiting organ transport distances. It works well when organs are high-quality: after a match run, high-quality organs are placed quickly because acceptance rates are high. However, the placement of lower quality livers can be challenging because OPOs must sequentially offer organs to a multitude of candidates who are listed at any number of the 152 US liver transplant centers. The process is slowed by the small number of centers (10) to which an offer can be made simultaneously and by the hour time period afforded for consideration and decision.

This protracted process for the placement of suboptimal-quality organs may incentivize expedited placement mechanisms outside OPTN policy that do not adhere to the computer-generated match run in order to facilitate national liver placement. Although one would expect that the pattern of offering and accepting national livers would generally mirror the national distribution of candidates by MELD score, the distribution of nationally placed livers is highly concentrated in 6 centers that accept two-thirds of nationally placed livers (high-importer centers). This has led to speculation about whether OPOs are using expedited placement mechanisms for the majority of national livers. Therefore, in this study, we aimed to characterize the offer pathways of nationally distributed livers in an effort to answer this question.

PATIENTS AND METHODS

Offer Data

Using data from the OPTN potential transplant recipient database, we evaluated all national offers of livers (n=91,483) that were ultimately placed nationally (n=1625) to adult wait-list candidates from February 1, 2005 through January 31, 2010. This study period corresponds to a 5-year period after the implementation of the Share 15 distribution policy, which dictates that livers are allocated first locally and then regionally to wait-list candidates with MELD scores ≥15 before they are offered locally to candidates with MELD scores <15. If a liver graft has been refused for all local and regional candidates, the graft is then offered nationally. Nationally distributed livers that were accepted on the first national offer were termed first-national-offer livers.

The characteristics of donors and recipients of nationally distributed livers during this study period have been previously reported. In this study, patients undergoing transplantation for fulminant hepatic failure were included. We described donor livers with the donor risk index (DRI), hepatitis C antibody status, split/partial liver status, and Centers for Disease Control and Prevention (CDC) high-risk status.

Data regarding donor, recipient, and center characteristics were obtained via the Standard Transplant and Analysis Research files from UNOS/OPTN as of June 30, 2010.

DSA, Center, and Regional Characteristics

Fifty-one DSAs were included in this study. New York, Ohio, and Tennessee were considered single DSAs because of regional sharing agreements. DSAs that exported ≥10% of their liver volume outside their region were categorized as high-exporter DSAs. DSAs were also categorized by the level of competition among transplant centers within each DSA with the quartiles of the Herfindahl-Hirschman index (no, low, medium, and high competition), which is a commonly accepted measure of market concentration. Only transplant centers that performed at least 5 adult liver transplants over the 5-year study period were included (n=113). Six high-importer centers were described in our previous study as accepting and transplanting 64% of all nationally placed livers during the study period. The 11 UNOS regions were categorized according to their median MELD scores at transplant [the liver transplant Model for End-Stage Liver Disease (LT-MELD) scores] into regions with low (regions 3, 6, 10, and 11), medium (regions 2, 4, 7, and 8), and high MELD scores (regions 1, 5, and 9).

Statistical Analysis

Descriptive continuous and dichotomous characteristics were compared with the Wilcoxon and chi-square tests as appropriate. Logistic regression was used to calculate the odds of a liver being offered to a higher priority candidate. Graft survival rates at 1 and 3 years were calculated with the Kaplan-Meier method and compared with the log-rank test. Cox regression models were used to calculate the risk of graft failure associated with transplantation with a first-national-offer liver. We evaluated recipient covariates (age, sex, race, hepatitis C virus diagnosis, and LT-MELD score), the DRI, the center volume, the DSA categorized by the median LT-MELD score, and the UNOS region in multivariate models. Covariates were selected for inclusion in the final multivariate model via backwards deletion with a cutoff of 0.05. We used robust standard errors with clustering by center and included the UNOS region as a fixed effect in the final model.

To investigate the existence of and to define preferred liver placement pathways, we developed Poisson random effects models to predict the expected numbers of first offers of national livers for each national pathway in each year from 2005 to 2009. National pathways are DSA–transplant center pairings in which the DSAs and the transplant centers are not located in the same region. To model the expected numbers of first national offers for each national pathway, we used fixed effects for the following time-dependent (per-year) covariates:

1. Volume of livers procured per DSA.
2. Volume of local transplants performed per DSA.
3. Median volume of the waiting list per DSA.
4. Volume of transplants performed per center.
5. Proportion of transplants with an LT-MELD score ≥30 per center.

These variables were selected because they each theoretically affect the number of offers that would be expected to arise from a specific DSA and to a specific center. To improve the fit, we used 3-knot cubic splines to model nonlinear effects of DSA and center volume, and we included an interaction between DSA volume and transplant center volume (all other interactions between covariates were evaluated and were not statistically significant). Then, to model differences between the observed and predicted numbers of first national liver offers, we included random effects for pathways, which was assumed to be normally distributed on a log mean scale. After fitting the model, we obtained best-fit linear unbiased predictions of these random effects and their standard errors. In the final step, we conservatively identified preferred pathways as those pathways that exceeded their best-fit linear unbiased predictions by more than 3 standard errors (\(z\)). Using this conservative criterion, we identified 97 preferred pathways. These procedures were implemented with the xtmepoisson command in Stata 12.2 (StataCorp., College Station, TX).

The institutional review board of the University of California San Francisco approved this study.

RESULTS

Characteristics of DSAs

There were 51 DSAs and 113 transplant centers included in the analyses. In general, each DSA placed livers at a median of 2 local transplant centers (interquartile range = 1-3, range = 1-8), at a median of 12 regional centers (interquartile range = 8-16, range = 3-17), and at a median of 102 national centers (interquartile range = 98-105, range = 96-110). At least 1 liver was placed nationally (n = 1625) from each DSA, but the proportion of all livers that were placed nationally per DSA ranged from 1% to 36% (Fig. 1).

Seven DSAs exported ≥10% of their liver volume nationally (high exporters), and they accounted for 46% of all national livers transplanted during the study period (Fig. 1). Six of the 7 high-exporter DSAs were located in regions with low LT-MELD scores; the other was located in a region with medium LT-MELD scores. None of the high-exporter DSAs included centers with high levels of competition within their DSA; in fact, 3 of the 7 DSAs served a single transplant center (ie, noncompetitive centers).

DSA-Center Pathways

For the 1625 national livers transplanted during the 5-year study period, 91,483 offers were made along a national distribution pathway. Of the 2830 possible DSA-center pathways for national liver offers, 2458 (87%) were used at least once. Each of the 7 high exporters used a single DSA-center pathway for 8% to 21% of their national liver offers.

In order to determine whether certain pathways were preferentially used for the very first offer of a nationally distributed liver, we estimated the expected occurrence of each specific DSA-center pathway on the basis of DSA characteristics (the number of livers that were procured within a DSA, the size of the wait list per DSA, and the number of local transplants performed within a DSA) and transplant center characteristics (the center volume and the proportion of transplants performed with an LT-MELD score ≥30 per center). Ninety-seven pathways met our conservative criterion for preferred pathways, and they accounted for 810 offers of national livers. Twenty-one of these pathways (22%) involved 1 of the 7 high-exporter DSAs and 1 of the 6 high-importer centers: 398 of the 810 offers (49%) used one of these preferred high-exporter DSA/high-importer center pathways (Fig. 3). One high-importer center was not involved in any preferred pathways from a high-exporter DSA. In comparison with first offers using nonpreferred pathways (n = 2361), first offers along a preferred pathway were offered to candidates with lower median LT-MELD scores (22 versus 36, P < 0.001) and to fewer status 1 candidates (19% versus 61%, P < 0.001).

First-National-Offer Livers and Their DSAs

On average, nationally placed livers were offered to a median of 5 patients (interquartile range = 1-21) at a median of 2 centers (interquartile range = 1-7). In all, 580 of 1625 livers (36%) were accepted on the first national offer (first-national-offer livers; Fig. 2); 423 of the 580 livers (73%) were transplanted at 1 of the 6 high-importer centers. The median number of offers for all other national livers (eg, those placed with more than 1 national offer) was 14 (interquartile range = 5-45) at a median of 5 centers (interquartile range = 2-12). The donor and transplant characteristics of livers placed with 1 national offer and livers placed with more than 1 national offer are shown in Table 1. The donors of livers placed with 1 national offer and the
donors of livers placed with more than 1 national offer were clinically similar, but they differed statistically in age (48 versus 51 years), positivity for hepatitis C virus antibody (7% versus 13%), diabetes (16% versus 20%), and aspartate aminotransferase levels (52 versus 45 IU/L). The DRI for first-offer livers was statistically but not clinically lower than the DRI for livers placed with more than 1 offer (2.0 versus 2.1). The median LT-MELD score was 19 for livers placed with 1 offer and 22 for livers placed with more than 1 offer.

Four DSAs placed 274 of 580 first-national-offer livers (47%). First-national-offer livers accounted for 42% to 58% of the total national liver placement volume for these 4 DSAs. A single center accepted 120 of 274 first-offer livers (44%) from these 4 DSAs. Although first-national-offer quality was similar ($P<0.2$; data not shown), the national offer patterns of these 4 DSAs differed significantly from all others (Table 2). First, these 4 DSAs exported their national livers with a median of 1 national offer, whereas the median number was 7 for all other DSAs. Second, only 25% of their national livers were first offered to status 1 candidates, whereas 47% were offered to these candidates in all other DSAs. The median LT-

**TABLE 1. Characteristics of Nationally Distributed Livers and Their Recipients Categorized by Placement With 1 National Offer Versus More Than 1 National Offer**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Livers Placed With 1 National Offer</th>
<th>Livers Placed With More Than 1 National Offer</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Donor age (years)*</td>
<td>48 (34–59)</td>
<td>51 (38–65)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Donor positive for hepatitis C virus antibody (%)</td>
<td>7</td>
<td>13</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CDC high-risk status (%)</td>
<td>11</td>
<td>14</td>
<td>0.08</td>
</tr>
<tr>
<td>Cause of death: stroke (%)</td>
<td>49</td>
<td>53</td>
<td>0.002</td>
</tr>
<tr>
<td>Donation after cardiac death (%)</td>
<td>8</td>
<td>10</td>
<td>0.10</td>
</tr>
<tr>
<td>DRI*</td>
<td>2.0 (1.6–2.4)</td>
<td>2.1 (1.7–2.5)</td>
<td>0.001</td>
</tr>
<tr>
<td>Donor diabetes (%)</td>
<td>16</td>
<td>20</td>
<td>0.03</td>
</tr>
<tr>
<td>Donor aspartate aminotransferase level (IU/L)*</td>
<td>52 (29–106)</td>
<td>45 (27–87)</td>
<td>0.02</td>
</tr>
<tr>
<td>Donor alanine aminotransferase level (IU/L)*</td>
<td>35 (22–74)</td>
<td>34 (21–69)</td>
<td>0.53</td>
</tr>
<tr>
<td>Status 1 (%)</td>
<td>7</td>
<td>3</td>
<td>0.001</td>
</tr>
<tr>
<td>LT-MELD score*</td>
<td>19 (14–24)</td>
<td>22 (16–27)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cold ischemia time (hours)*</td>
<td>9 (7–11)</td>
<td>9 (7–11)</td>
<td>0.05</td>
</tr>
</tbody>
</table>

*The data are presented as medians and interquartile ranges.

**TABLE 2. Comparison of 4 DSAs That Exported High Numbers of Livers With 1 National Offer Versus All Other DSAs**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>OPOs Placing High Percentage of Livers With 1 National Offer*</th>
<th>Other OPOs†</th>
</tr>
</thead>
<tbody>
<tr>
<td>National offers per national liver†</td>
<td>1 (1–10)</td>
<td>7 (1–27)</td>
</tr>
<tr>
<td>Livers offered first to status 1 candidates (%)</td>
<td>25</td>
<td>47</td>
</tr>
<tr>
<td>LT-MELD score of OPOs‡</td>
<td>22 (18–25)</td>
<td>25 (22–31)</td>
</tr>
<tr>
<td>LT-MELD score of first national offer for each nationally placed liver†</td>
<td>22 (16–28)</td>
<td>28 (18–40)</td>
</tr>
<tr>
<td>LT-MELD score of national liver recipients procured by OPOs‡</td>
<td>18 (14–23)</td>
<td>22 (15–27)</td>
</tr>
</tbody>
</table>

NOTE: $P<0.001$ for all comparisons.

*Four OPOs and 542 livers.
†Forty-seven OPOs and 1083 livers.
The data are presented as medians and interquartile ranges.
The unadjusted 1-year survival rates for livers placed on 1 national offer and livers placed on more than 1 national offer were 72% and 80%, respectively, and the 3-year survival rates were 61% and 67%, respectively. In the univariate analysis, transplantation with a liver placed on 1 national offer was associated with a 26% increased risk of graft failure in comparison with transplantation with a liver placed on more than 1 national offer (hazard ratio = 1.26, 95% confidence interval = 1.05–1.50, P = 0.01). After adjustments for factors significantly associated with graft failure in multivariate models (recipient age, LT-MELD score, DRI, region, and clustering by center), transplantation with a liver placed on 1 national offer was associated with a 36% increased risk of graft failure in comparison with transplantation with a liver placed on more than 1 national offer (hazard ratio = 1.36, 95% confidence interval = 1.12–1.66, P = 0.001). There was no difference in graft survival between high-importer centers and all other centers: for livers accepted on the first national offer, the 1- and 3-year graft survival rates were 73% and 62%, respectively, for the 6 high-importer centers and 69% and 61%, respectively, for all other centers (P = 0.70). There was no difference in the 30-day retransplantation rate for nationally placed livers accepted on 1 offer versus livers accepted on more than 1 offer (4% versus 3%, P = 0.09), nor was there a difference in the 30-day retransplantation rate for high-importer centers versus all other centers (4% versus 4%, P = 0.8).

DISCUSSION

In this study evaluating offer patterns of nationally placed livers by DSAs, we found that the placement patterns of national livers varied widely by DSA. In fact, nearly half of the nationally placed livers were procured within 7 DSAs during the 5-year study period. These DSAs were located in UNOS regions with low LT-MELD scores, as one might have predicted. Several of our findings were, however, provocative. First, 21 first-national-offer pathways involving the 7 high-exporter DSAs and 5 of the 6 high-importer centers were used at an unexpectedly high frequency. These represent preferred pathways between these DSAs and centers. Second, a high proportion of nationally placed livers were accepted on the very first national offer. Because the median MELD score of national liver recipients is modest at 20,3 one would have expected that before percolating down to a patient with a MELD score of 20, a liver offer would have to be refused by many candidates (tens and potentially hundreds) with higher MELD scores. Instead, we found that more than one-third of all
national livers were placed with a single offer. Approximately half of these first-national-offer livers originated within only 4 DSAs; nearly three-quarters were accepted by only 6 previously identified high-importer centers.3

Because of the negative synergistic effect of matching low-quality organs with high-MELD-score recipients, the centers accepting these livers are likely making smart decisions for their centers and patients. However, the relatively low MELD scores of the candidates receiving first liver offers raise concerns about the patients and physicians at the bypassed centers who never had the opportunity to make decisions regarding these offers in accordance with our established MELD allocation system. Although a high-MELD-score patient may not be the best candidate for a low-quality, nationally distributed liver, a low-MELD-score patient may not derive greater survival benefit than a mid-MELD-score patient who has both a higher risk of wait-list mortality (in comparison with a low-MELD-score patient) and a lower probability of receiving another timely liver offer (in comparison with a patient with a higher MELD score). These presumably bypassed, mid-MELD-score patients may be at the greatest disadvantage from this practice of expedited placement.

It is interesting that the national livers that were accepted on the very first national offer were associated with a higher adjusted risk of graft loss. We were unable to determine significant differences in donor or recipient characteristics with the UNOS registry data that could explain these worse-than-expected outcomes. We speculate that these livers may have been significantly lower in quality in ways that are not reliably captured by UNOS variables, such as severe macrosteatosis, the need for rapid placement (because the livers were already procured but were refused), or anatomic abnormalities.

Is it possible that this DSA-center pattern emerged because the 6 high-importer centers consistently had the candidates with highest MELD scores in the match run at the time of the national liver offers? Because we do not have the necessary data to prioritize all wait-list candidates at the time of each liver offer, we cannot conclude definitively that the patient who received the first liver offer was not the highest priority candidate at that time; this is a limitation of the available data and, therefore, our study. However, compared to livers originating from other DSAs, national livers originating from 1 of the 4 high-exporter, preferred-pathway DSAs were less likely to be offered first to a status 1 candidate; they were also less likely to be transplanted into a recipient with an LT-MELD score higher than that of the originating DSA. We would have expected livers that were refused on the local and regional levels to first be offered to the candidate with the top LT-MELD score nationally. With 3 definitions of expedited [(1) modeled preferred pathways, (2) high-exporter DSAs/high-importer centers, and (3) livers accepted on the first national offer], our data evidence the existence of expedited placement pathways and allow for some description of the practice.

New Policy Proposal for Out-of-Sequence Allocation

Matching donors with recipients is a time-sensitive process because there is a finite period of donor management before it becomes medically necessary to recover organs for transplantation. After a period of receiving multiple sequential declinations along the predetermined match run, the offer process becomes cumbersome and time-consuming. In such instances, the OPO that governs the DSA, whose performance is measured in part by its organ placement rates, has an incentive to initiate an out-of-sequence allocation by offering the liver to transplant centers that are more likely to accept it on the basis of historical decision-making patterns. Although this process may facilitate the efficient placement of the liver and thus prevent discard, it bypasses candidates who have higher disease severity than the final accepting recipient and potentially deprives patients of the opportunity for liver transplantation with that specific liver. Because it is based on the liver offer acceptance history of the transplant center, it is center-centric rather than patient-centric. Out-of-sequence allocation lacks transparency and is inherently unfair to the bypassed candidates.

Currently, no OPTN policy governs out-of-sequence allocation. We propose a new policy that explicitly and transparently allows for expedited placement but does not skip patients with the greatest need. When a liver has been refused on local and regional levels, all centers that have indicated interest in accepting a national liver would be notified of its availability. These pre-identified, interested centers would, in real time, have the opportunity to specify patients with the highest allocation priority for whom they would accept an offer. All of these centers would be required to take action within the same hour (or some prespecified timeframe) of the liver offer. At the end of this timeframe, the offer process would close, and the liver would automatically be allocated to the highest priority candidate among all interested centers. If a center does not respond within the timeframe, then it is not eligible to receive the liver offer. Because the liver is offered to all systems simultaneously, the number of centers participating at a given time will not affect the expedience of placement. This system would be completely voluntary so that centers that are unable or uninterested in using nationally placed livers would not have to participate. Alternatively, they could choose to selectively participate to facilitate transplantation for a specific patient or a specific type of patient such as a status 1 patient in particular need.

We anticipate that the implementation of this system will increase the average MELD score of national liver recipients because centers will be incentivized to specify patients with higher MELD scores in order to receive liver offers. However, because centers will still
be judged by transplant program–specific reports based on their wait-list and posttransplant outcomes, we believe that centers, knowing the specific details of a liver offer and the need of a specific patient, will participate in a specific liver offer only for patients for whom they can reasonably achieve acceptable posttransplant outcomes. The practice of accepting a liver on behalf of a patient with a very high MELD score will also be tempered by the financial incentive to reduce costs because the transplantation of high-DRI livers into patients with high MELD scores synergistically increases costs. There will still be a strong incentive to participate in this system on behalf of patients whose disease burden exceeds their MELD score because these patients have a mortality risk that is not captured by their MELD score (eg, refractory hepatic hydrothorax, refractory encephalopathy, or hepatocellular carcinoma outside the Milan criteria) and thus are more likely to die on the wait list before receiving another liver offer.

The OPOs that govern DSAs serve a vital function in the national organ transplantation effort. They have the responsibility to maximize organ procurement and transplant efforts on behalf of all deceased donors and their families. The implementation of our proposed policy for out-of-sequence allocation would facilitate placement efforts and help to balance the efficiency, equity, and transparency of the process for all wait-listed candidates.

REFERENCES