Research Article

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Liver transplant center variability in accepting organ offers and its impact on patient survival

David S. Goldberg[1,2,3,*], Benjamin French[2,3], James D. Lewis[1,2,3], Frank I. Scott[1,2], Ronac Mamtani[4], Richard Gilroy[5], Scott D. Halpern[2,3,6], Peter L. Abt[7]

[1]*Division of Gastroenterology, Department of Medicine, University of Pennsylvania, USA;* [2]*Center for Clinical Epidemiology and Biostatistics, Perelman School of Medicine at the University of Pennsylvania, USA;* [3]*Leonard Davis Institute of Health Economics, University of Pennsylvania, USA;* [4]*Division of Hematology and Oncology, Department of Medicine, University of Pennsylvania, USA;* [5]*Division of Gastroenterology, Department of Medicine, University of Kansas Medical Center, Kansas City, KS, USA;* [6]*Division of Pulmonary, Allergy, and Critical Care, Department of Medicine, University of Pennsylvania, USA;* [7]*Division of Transplantation, Department of Surgery, Hospital of the University of Pennsylvania, Philadelphia, PA, USA*

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Background & Aims: Despite an allocation system designed to give deceased-donor livers to the sickest patients, many transplantable livers are declined by U.S. transplant centers. It is unknown whether centers vary in their propensities to decline organs for the highest priority patients, and how these decisions directly impact patient outcomes.

Methods: We analyzed Organ Procurement and Transplantation Network (OPTN) data from 5/1/07-6/17/13, and included all adult liver-alone waitlist candidates offered an organ that was ultimately transplanted. We evaluated acceptance rates of liver offers for the highest ranked patients and their subsequent waitlist mortality.

Results: Of the 23,740 unique organ offers, 8882 (37.4%) were accepted for the first-ranked patient. Despite adjusting for organ quality and recipient severity of illness, transplant centers within and across geographic regions varied strikingly (p <0.001) in the percentage of organ offers they accepted for the highest priority patients. Among all patients ranked first on waitlists, the adjusted center-specific organ acceptance rates ranged from 15.7% to 58.1%. In multivariable models, there was a 27% increased odds of waitlist mortality for every 5% absolute decrease in a center's adjusted organ offer acceptance rate (adjusted OR: 1.27, 95% CI: 1.20–1.32). However, the absolute difference in median 5-year adjusted graft survival was 4% between livers accepted for the first-ranked patient, compared to those declined and transplanted at a lower position.

Conclusion: There is marked variability in center practices regarding accepting livers allocated to the highest priority patients. Center-level decisions to decline organs substantially increased patients' odds of dying on the waitlist without a transplant.

Keywords: Organ offer; Decline; Waitlist mortality.

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* Corresponding author. Address: Blockley Hall, 423 Guardian Drive, Room 730, Philadelphia, PA 19104, USA. Tel.: +1 215 746 8598; fax: +1 215 349 5915.

E-mail address: david.goldberg@uphs.upenn.edu (D.S. Goldberg).

Abbreviations: OPTN, Organ Procurement and Transplantation Network; MELD, Model for End-Stage Liver Disease; UNOS, United Network for Organ Sharing; HCC, hepatocellular carcinoma; DRI, donor risk index; LSAM, Liver Simulated Allocation Model.

Introduction

Prioritization on the liver transplant waitlist follows an urgency-based (i.e., 'sickest-first') model. Urgency-based prioritization aligns with the 'Final Rule' proposed by the US Department of Health and Human Services in 1998 [1]. Since 2002, the Model for End-Stage Liver Disease (MELD) score, an objective measure that strongly predicts the risk of death on the waitlist [2], has been used to prioritize patients and allocate organs. All patients actively listed are determined by a center as being well enough for transplantation at the time of an organ offer. With few exceptions, organs are first offered based on the MELD score, first locally among liver transplant programs within the 58 donor service areas, then regionally to a greater number of programs among the 11 United Network for Organ Sharing (UNOS) regions, and then nationally to all programs.

Despite MELD-based allocation [3], geographic differences in waitlist mortality rates exist [4–9]. These differences have been attributed to variations in organ supply as compared to waitlist demand. Proposals to redraw lines of organ distribution in order to improve equity are under review, and have generated considerable discussion [5], including by members of Congress whose support is divided by geography rather than political party lines [10,11]. However in all of these discussions, little attention has been given to an alternative potential source of differences in waitlist mortality: differential utilization of available organs by transplant centers. Previous data has suggested that transplant centers differ in average "quality" of the liver allografts transplanted, with higher-volume centers and centers with more local competition using higher-risk organs [12]. Furthermore, six liver

transplant centers (out of nearly 110 in the US) utilize 64% of all nationally placed allografts (livers transplanted outside of the UNOS region of procurement) [13]. An explanation for this is that many factors beyond the organ that is being allocated also may influence the decision to accept an offer [14].

Despite our current knowledge of organ utilization among centers, there are limited data defining how often organ offers are accepted for those sickest patients most in need (the highest priority patients), how often organs are declined by centers, how centers differ in their acceptance behavior, and how these behaviors influence the probability a patient will be transplanted successfully, die after transplant, or die on the waitlist [15,16]. We sought to evaluate: 1) within and across-region center variability in center acceptance patterns for livers offered to the highest-prioritized patients; 2) factors associated with offer acceptance; and 3) the association between center behavior on patient outcomes.

Patients and methods

US organ allocation system

The organ transplant system in the US is managed by UNOS. For the purposes of organ donation and allocation, the US is divided geographically at two levels. There are 11 'regions', with each region (except for region 9) encompassing multiple adjacent states (e.g., region 2 includes Pennsylvania, Delaware, New Jersey, Maryland, Washington D.C., and West Virginia). Second, regions are subdivided into 58 smaller geographic units (donor service areas). Donor service areas vary in land area and population size, but are the local unit by which organs are procured and allocated, with one organ procurement organization in each donor service area responsible for procuring donor organs. For example, in region 2, there are five donor service areas that do not necessarily follow state boundaries. With certain exceptions, organs are first offered to patients in the same donor service areas as the donor. If not accepted for patients in the same donor service area, the organ is next offered to patients in the same region. It must be noted that although the performance of transplant centers in the US is closely tracked, with potential penalties for outcomes that are lower than expected, these do not include any penalties for declining organ offers for a given patient.

Match run waitlist mechanics

Each time a deceased-donor liver becomes available, UNOS ranks all patients eligible to receive the organ based on the donor and potential recipient's blood type, the potential recipient's geographic location, most recent MELD score, and potential recipient's willingness to accept organs from donors with certain characteristics (e.g., is the patient willing to accept an organ from a donor with hepatitis C, or a donor over a certain age). The organ is then offered to the center at which the highest ranked patient is waitlisted. This is referred to as the match run. With few exceptions, organ offers follow a sequential process (Supplementary Figs. 1 and 2). A center, and specifically the on-call transplant surgeon, could decline an offered organ for several reasons: donor quality (e.g., donor age), recipient clinical status, donor-recipient size mismatch, or the opinion that a patient with lower priority has a greater risk of death. When an organ offer is declined for the highest ranked patient, that patient will either be transplanted after a future offer is accepted, or die without being transplanted (with or without receiving subsequent offers). The rank list is dynamic, changing daily as new patients are added, existing patients removed, and MELD scores are updated. As such, the decision to decline an organ offer for the highest ranked patient does not assure that the same patient will be ranked at or near the top when the next organ is available.

Study sample

Using data from the Organ Procurement and Transplantation Network (OPTN)/UNOS, this study evaluated match runs for livers from May 1, 2007, the first date of available match run data, through June 17, 2013. Match run data were only available for livers that were ultimately transplanted.

We excluded match runs in which the highest ranked patient was <18 years of age or a multi-organ transplant candidate; the organ offer was bypassed to a lower ranked patient (e.g., directed donation where the donor's next-of-kin specify their recipient of choice); or critical donor data (e.g., age) were missing. Transplant centers with patients ranked first on a match run <20 times/year were excluded because their acceptance patterns could be artificially variable due to small sample sizes (6/110 transplant centers with a total of 305 match runs with a patient ranked first during the study period).

Outcomes

In analyses evaluating center variability in organ offer acceptance rates, the outcome was whether the offer was accepted for a given patient. The first-ranked patient for each offer was the unit of analysis, aggregated by center to calculate that center's acceptance rate (Supplementary Fig. 2). For models assessing waitlist mortality, the outcome was waitlist removal for death or clinical deterioration, which included dying on the waitlist, or removal for being 'too sick to transplant,' or for 'other' reasons with a known date of death within 90 days of removal, based on Social Security Death Master File data [4,17]. Waitlist removal was modeled as a binary outcome given the short time interval from initial organ offer to waitlist removal date (median 10 days; 72.9% of removals for death or clinical deterioration occurring within 30 days of an organ offer being declined, and 81.5% within 60 days) between being ranked first and subsequent outcomes of death or transplantation (the outcome in >95% patients ranked first) [17,18]. Lastly, we evaluated the graft-specific outcome of graft failure (recipient death or re-transplantation [19]).

Covariates

Recipient covariates included: age, sex, allocation MELD score (the higher value of the calculated or exception MELD score), race/ethnicity [20], previous liver transplantation, and receipt of hepatocellular carcinoma (HCC) or other exception points (which increase a patient's priority beyond their calculated MELD score [20]). Donor covariates included: sex, height, weight, age, race/ethnicity, cause of death, donation after cardiac death status (in contrast to standard brain-dead donors, these grafts have more ischemic injury and inferior outcomes [21–23]), and share type. Share type refers to the geographic location of the donor with regards to the patient offered the organ: a) donor service area (local unit of organ allocation); b) statewide-share; or 3) regional-share (same UNOS region). Local transplant center density was modeled as the number of liver transplant centers within a donor service area. We did not adjust for blood type in organ acceptance models as donor organs are only offered to waitlist patients of the same blood type (or compatible for recipient blood group AB or B under specific circumstances).

Statistical analysis

Center acceptance rates

Mixed-effects logistic regression models with patient- and center-level random intercepts were used to quantify and test for variability in acceptance rates across transplant centers after adjustment for recipient and donor characteristics among all included match runs. Individual patients are clustered (or grouped) within transplant centers, which could lead to correlated outcomes of patients within those clusters. In contrast to a traditional fixed effect (i.e., gender, age, race, ethnicity) that has levels that are of primary interest and would be used again if the study were repeated, random effects can be viewed as selecting from a much larger set of levels [24]. In the case of this study, centers serve as the random effects, because one can view the centers in this study as being selected from the set of all transplant centers.

In the case of this study, the primary models were multi-level, because there were two levels of clustering: patients within centers; and individual patients themselves, because patients could have more than one organ offer, and thus, acceptance decisions could be correlated among patients within centers, and among individual patients with multiple offers [24]. In these mixed-effects models, the null hypothesis was that there was no residual heterogeneity (e.g., after accounting for all of the covariates in the model, the acceptance rates among centers are statistically not different from one another). A p value <0.05 suggested that there were significant differences in organ offer acceptance rates after adjusting for the observed covariates in the model [25]. We conducted a hypothesis test that the standard deviation of the center-level random intercepts was equal to 0 using a likelihood ratio test, comparing a model that included both patient- and center-level random intercepts to a model that included only patient level random intercepts. Due to the limitations of this approach [26], we also