# High risk liver transplant recipients with grade 3 acute on chronic liver failure should receive good quality graft

**Short title:** ACLF-3 and Liver Transplantation

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**Abbreviations** (in order of appearance in the manuscript): ACLF: Acute on chronic liver failure; LT: Liver transplantation; UNOS: United network for organ sharing; EASL-CLIF: European association for study of liver disease-chronic liver failure; ALD: Alcohol-associated liver disease; DRI: Donor risk index; MELD: Model for end-stage liver disease.

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## ABSTRACT

**Background and Aim**: We aimed to develop a risk score for LT recipient and donor selection among patients with ACLF-3. **Methods and Results**: 7166 adult LT recipients (mean age 53 years, 63% males, 56% Caucasians, 42% obese, median MELD score 36.5) using deceased donor grafts in the UNOS database (01/2002-06/2018) who were in ACLF-3 at LT as per EASL-CLIF criteria were analyzed. Cox regression model on the derivation dataset (N=3583) showed recipient age, non-alcohol etiology, pulmonary failure, brain failure, and cardiovascular failure to be associated with 1-yr. patient survival. Observed and expected post-transplant 1-yr. survival showed excellent correlation (R=0.920). Risk score from cox model on derivation dataset stratified 3583 recipients in validation cohort using cut-off score 7.55 and 11.57 to low (N=1211), medium (N=1168), and high risk (N=1199), with 1-yr patient survival of 89%, 82%, and 80% respectively. Based on poor vs. good quality graft (donor risk index cut-off at 1.50), 1-yr. patient survival for low, medium, and high risk categories were 90 vs. 89% (P=0.490), 83 vs. 82% (P=0.390), and 83 vs. 78% (P=0.038) respectively. Among recipients with high risk score, donor factors of age ≥60 yrs., grafts obtained from national sharing, and macro-steatosis >15% were associated with 1-yr. patient survival below 66%. **Conclusion**: Among ACLF-3 liver transplant recipients, those with high risk at the time of transplant receiving better quality graft will improve post-transplant outcomes. Prospective studies using additional characteristics are needed to derive accurate risk score model in predicting post-transplant outcomes among recipients with ACLF-3.

**Key Words:** ACLF; Cirrhosis; Mortality; Organ failure; Survival; UNOS

## Lay Summary

Among patients with cirrhosis, the presence of multi organ failure, a condition referred to as acute on chronic liver failure has poorer outcomes after receiving liver transplantation. Quality of the deceased donor graft is an important determinant of post-transplant outcomes. This study describes and validates a new scoring method that can be used to match recipients and donors among severe forms of acute on chronic liver failure with 3 or more organ failures, and optimize the post-transplant outcomes.

Acute on chronic liver failure (ACLF) occurs in 5-30% of hospitalized patients with cirrhosis, and has a mortality rate of 25-42% and 40-56% at 28 and 90 days respectively [1-5]. Liver transplantation (LT) among select ACLF patients provides survival benefit [6-10]. However, patients with ACLF-3 with three or more organ failures have poorer outcomes compared to less severe ACLF or patients with decompensated cirrhosis without ACLF. Criteria on patient selection for LT, especially for ACLF-3 patients are scanty. In a recent report using the UNOS database, pulmonary failure, donor risk index, and waiting period of more than 30 days on the LT list emerged as predictors of post-transplant outcome among transplant recipients with ACLF-3 at LT.[6] We performed this study using the UNOS database on a cohort of patients with ACLF-3 selected to receive LT, with an aim to develop a risk score, which could be used to select and allocate donor livers as basis of optimizing post-transplant patient survival.

## METHODS

### Study population

United Network for Organ Sharing (UNOS) database (01/2002 to 06/2018) was used to extract a cohort of adult (≥18 years of age) LT recipients using deceased donor liver graft. Listings for concomitant hepatocellular carcinoma or HCC (4400.4 4401, 4402), acute liver failure or status 1A, or with previous LT were excluded. LT recipients were stratified to ACLF and its grade at LT using modified European Association for the Study of the Liver (EASL)-Chronic Liver Failure [CLIF] (EASL-CLIF) criteria, **Supplementary Tables 1 and 2** [5]. Patient's functional status at LT using the Karnofsky's performance status scale (KPSS) was stratified to 1 (80-100%), 2 (60-70%), 3 (40-50%), and 4 (10-30%), with 1 being the best and 4 worst functional status.[11]

### Data collection

Data on the study cohort was extracted on a) recipients for demographics (age, gender, race, BMI); liver disease etiology; comorbidities (diabetes mellitus and obesity); organ failure and

severity of ACLF; KPSS; and survival status at one year after LT and b) donors for all the variable included in donor risk index (DRI) and graft steatosis among the biopsied grafts

**Study Outcome**

The study outcome was one year patient survival after LT as used in ours and other studies previously in patients with ACLF.[10,12,13]

## Data and statistical analyses

Kaplan Meier curves were generated stratified for ACLF and its grade at the time of LT for patient survival at one year after LT. Patients surviving at one year were censored, and Log Rank statistical test was used for this analyses.

A cohort of LT recipients with ACLF-3 at the time of LT was further analyzed. Using a split sample validation technique, this cohort was randomly split into a derivation dataset and a validation dataset. Both datasets were compared for baseline characteristics using chi-square and analysis of variance for categorical and continuous variables respectively. Cox proportional hazard regression model was built on the derivation dataset to derive independent predictors of 1-yr. patient survival after LT. Recipient variables at the time of LT including demographics (age, gender, and race), liver disease etiology, type of organ failure, MELD score, progression of ACLF grade from the time of listing, and KPSS were entered in the model. Backward elimination procedure was used to derive final model and the variables predictive of 1-yr. patient survival. As number of organ failures and extrahepatic organ (ventilator, cardiovascular, and brain) failures are more relevant in predicting survival, [6,10] two other models were tested in the derivation dataset, replacing type of organ failure with number of organ failures (4-6 vs. ≤3 organ failures) or with extrahepatic vs. no extrahepatic organ failure. C-statistics and area under the receiver operating characteristics curve were derived on these models, using the method for time dependent receiver operating characteristic curves for censored survival data.[14] As the study period is long (2002-2018) with the study population characteristics changing over time,

we also included study period era (2002-2006, 2007-2011, 2012-2018) into the final most accurate model based on the c-statistics.

The parameter estimates of the most accurate model on the derivation dataset were used to derive a risk score for 1-yr. patient survival after LT. Based on the tertiles of this risk score, LT recipients were stratified to low, medium, and high risk for patient mortality at 1-yr. after LT. The risk score was applied to the validation dataset and Kaplan Meier survival curves were generated based on the risk stratification. Patients surviving at one year were censored, and Log Rank statistical test was used for survival analyses. Observed 1-yr. survival was also calibrated against the expected frequencies for model goodness of fit and their correlation.

To show performance of score algorithm, we further analyzed 1-yr. patient survival for the three risk score categories based on liver graft quality, which was stratified using the median DRI in the dataset. Recognizing that DRI was developed in 2006 using the data before the MELD era and may not be relevant to select donors in today's era,[15] we focused on individual donor characteristics built into deriving the DRI and their impact on the post-transplant 1-yr. patient survival. Significant results were further examined for specific components of the DRI. Although fat content of graft or steatosis is not a component of DRI, but as this is known to impact the post-transplant patient outcomes,[16] we examined 1-yr. patient survival for graft steatosis in a subgroup of patients receiving grafts which were biopsied and had information on graft steatosis. SAS version 9.4 (SAS Institute, Cary, NC, USA) was used for statistical analyses, with P-values $< 0.05$ considered significant. As the study used a publicly available database with de-identified data, the study was exempt from Institutional Review Board approval.

## RESULTS

### Study Population

Of 54,956 LT recipients between 01/2002 and 06/2018, 23,947 (43.6%) with ACLF at the time of LT formed the study population and analyzed. Of these, 5559 (10.1%) recipients died within one

year after LT. Survival rates were 88.2%, 88.3%, and 83% for recipients with grade 1-3 ACLF at the time of LT respectively (**Supplementary Figure 1**). In a multivariable cox proportional hazard regression model, the risk of patient mortality at one year after LT was 34% and 24% higher for LT recipients with ACLF-3 at LT vs. ACLF-1 and ACLF-2 respectively. Survival of ACLF grade 2 vs.1 at LT was similar (Supplementary Table 3).

Further analysis is on 7166 LT recipients with ACLF-3 (mean age 53 years, 63% males, 56% Caucasians, 42% obese, median MELD score 36.5) at the time of LT. The underlying liver disease etiology was hepatitis C virus infection in 33%, alcohol-associated liver disease (ALD) in 30%, and non-alcoholic steatohepatitis in 11%. Of organ failures, liver renal failure were most common in 85% each followed by coagulation failure in 66%, brain failure in 53%, cardiovascular failure in 48%, and pulmonary failure in 13% (**Table 1**). At the time of listing, 37% were in ACLF-3 and 63% progressed from without ACLF (31%) or lesser grades of ACLF (ACLF-1 in 7%, and ACLF-2 in 25%).

### Deriving score to risk stratify patients for 1-yr. patient survival with ACLF-3 at LT

Derivation and validation datasets derived from random splitting of cohort of 7166 recipients with ACLF-3 at LT were similar on baseline characteristics (**Table 1**). Cox proportional multivariable hazard regression model on the derivation dataset showed recipient age, non-ALD etiology, pulmonary failure, brain failure, and cardiovascular failure as independent predictors of 1-yr. post-transplant patient survival (**Table 2**). Univariate models for each variable were also performed (Supplementary Table 4).

Two other models were examined replacing type of organ failure by number of organ failures (4-6 vs. ≤3) in one and extrahepatic vs. no extrahepatic organ failure in the other **(Table 2**). The c-statistics of three models were 0.603, 0.576, and 0.582 respectively (Supplementary **Figure 2 A-C**). Further analyses were performed using the model with type of organ failure. Results

remained similar after including study period era into the final model (Supplementary Table 5) with c-statistics of 0.628 (Supplementary Figure 3). As availability of direct acting antiviral drugs for HCV infection in the most recent era has improved the post-transplant outcome of patients with HCV, we also did a sub-analysis stratifying etiology of liver disease to HCV vs. non-HCV instead of alcohol vs. non-alcohol etiology. The results remained similar (Supplementary Table 6) with the model c-statistics of 0.623 (Supplementary Figure 4).

**Validation of score to risk stratify recipients for 1-yr. patient survival with ACLF-3 at LT**

The model was validated with calibration of deciles on observed frequencies on one year patient survival against deciles on expected frequencies validated this model, R coefficient 0.92 (**Figure 1A**). The parameter estimates from the cox model including the type of organ failure on the derivation dataset (N=3583) were applied to the validation dataset (N=3583) to develop a risk score equation was developed *int ((recipient age-20/5) + 5.2*pulmonary failure (0 or 1) + 4.7*brain failure (0 or 1) + 3.6*cardiovascular failure (0 or 1) + - 4.9*ALD etiology).* Based on the tertiles of this risk score, LT recipients were stratified for 1-yr. patient survival to low risk (N=1211, risk score <7.55), medium risk (N=1168, risk score 7.55-11.57), and high risk (N=1199, risk score >11.57). Kaplan Meier survival curves comparing the three risk categories showed one year patient survival rates of 88.9%, 82.1%, and 80.1% for risk strata of low, medium, and high respectively, Log Rank P<0.001 (**Figure 1B**). With a median (range) score of 9.7 (-3.9 to 23.5), the score was inversely associated (R = -0.59) with one-year median (range) predicted patient survival of 85.4% (67.5-99.4), Supplementary **Figure 5**.

**Donor risk index and 1-yr. patient survival**

A total of about 96% (3441 of 3583 in the validation dataset and 6894 of 7166 in the whole dataset) LT recipients had available data on DRI. Based on the median (interquartile range) DRI in both validation and whole datasets of 1.46 (1.29-1.71), the graft quality was stratified to good or poor at DRI cut-off 1.50, with good quality graft as DRI<1.5 and poor quality graft as

DRI>/=1.5. Within the validation and whole datasets, respective patient survival rates were similar comparing good vs. poor quality graft for recipients at low risk (90.3 vs. 89.1%, P=0.490 and 90.4 vs. 88.4%, P=0.120) and at medium risk (83.3 vs. 81.6%, P=0.39 and 84 vs. 81.3%, P=0.069). In contrast, outcome was better if good quality graft was used for recipients with high risk score (82.7 vs. 77.9, P=0.038 and 81.3 vs. 74.3, P<0.001), **Figure 2 A-B**.

Analysis of the whole cohort of recipients for 1-yr. patient survival after LT was further explored to examine impact of specific components of the DRI on 1-yr. patient survival within each risk category. Continuous variables (donor age, cold ischemic time, and donor height) were stratified to three groups (Supplementary Table 7). Within the high risk cohort, patients receiving grafts from donor ≥60 years of age or from national sharing had worse outcomes with 1-yr. patient survival of 66% and 63.8% respectively (**Table 3 and Figure 3 A-B**).

In a sub-cohort of 544 recipients with available data on graft macro-steatosis, comparing 108 recipients using grafts with ≥15% vs. 436 with <15% macro-steatosis were 61.1% and 76.2% respectively, Log Rank P=0.002 (**Figure 4**). As biopsy may be performed in grafts suspected of poor quality, we compared DRI among biopsied vs. not biopsied. DRI was higher among biopsied grafts, 1.66 +/- 0.35 vs. 1.49 +/- 0.30 with median (IQR) values of 1.63 (1.39-1.89) vs. 1.42 (1.27-1.65) respectively, P<0.001. As the traditional cut-off for macro steatosis is 30%, we revised the analysis using this cut-off. Results remained similar with patient survival at 1 yr. comparing graft steatosis >/=30 (N=33) vs. <30% (N=511) steatosis of 58 vs. 74%, Log Rank P=0.023.

## DISCUSSION

This study describes and validates a clinical scoring system to risk stratify patients undergoing LT for 1-yr. patient survival among recipients with grade 3 ACLF at the time of LT. Further, among those with high risk score, grafts from older donors, national sharing, and those with macro-

steatosis over 15% should be avoided. These data have important clinical relevance as the use of this scoring system may allow optimal use of the scarce donor pool.

Short-term mortality among patients with ACLF and multi-organ failure can be as high as 80%. LT provides survival benefit, with patient survival at one year after LT of 83% in ACLF-3, and 78% even in sickest patients with high risk score category. These observations are in concordance with another study using the UNOS data with 82% survival in ACLF-3 patients [6]. Among other single center studies, survival rate at one year after LT among recipients with ACLF-3 have varied between 43% and 84% [9,17-19]. In a recent multicenter European retrospective study on 308 consecutive ACLF patients, 234 received LT with 1-yr. patient survival rates of 81%, varying from 78.9% for grade 3 and 88.6% for grade 1 ACLF respectively.[13] These wide variations clearly reflect lack of clear criteria for patient selection as basis for optimal utilization of donor pool.

In the final model, alcohol as liver disease etiology was associated with better patient survival at one year, while variables at the time of LT of recipient age, pulmonary failure, cardiovascular and brain failure were associated with worse patient survival at one year after LT. Better post-transplant survival among recipients for alcohol-associated liver disease have been shown, probably due to younger age of these patients.[20-22] In another study, age cut-off of 57 years at the time of LT was associated with 50% worse post-transplant survival [9]. Similarly, mechanical ventilation and pulmonary failure has also been shown to be associated with worse post-transplant survival [6,7,23] As observed in previous studies, MELD and MELD-Na scores or its components were not associated with post-LT outcomes in our final model, confirming that MELD and MELD-Na do allow risk stratification of post-LT outcomes.[6,10] However, none of these studies aimed to derive a risk score to predict post-LT patient survival and match recipients with donor graft. Further, the association of brain failure (grade 3 or 4 hepatic encephalopathy) at the time of LT with worse post-transplant survival as shown in our study has not been reported earlier. It is

possible that concomitant ventilation in patients with stage 3-4 encephalopathy may be a confounding factor.

Using the independent factors associated with risk of death, we developed and validated risk score to identify patients with good outcomes after LT, with 88-91% one year recipient survival after LT among patients with lowest risk category. These survival rates are as good as patients with no or ACLF grade 1. As reported earlier in several studies [6,24,25], we observed an association of DRI and graft quality with the post-transplant patient survival at one year among recipients with ACLF at the time of LT. Regarding the specific components of DRI, we showed that recipients with grafts from donors aged 60 years or more or from national sharing had poor outcomes. A graft with mild macro steatosis (5%-30%) is considered acceptable for LT even if obtained from donors with cardiac death.[26] In this study, we showed that use of grafts with macro-steatosis over 15% significantly impacts 1-yr. patient survival and should preferably be avoided among high risk transplant recipients with ACLF-3.

Recently, another validated score using granular data on LT for ACLF 3 from five different centers has been shown to be accurate with c-statistics of 0.84. This simple score was based on four categorical pre-transplant variables (0 or 1 score assigned to each), age ≥53 years, arterial lactate of ≥4 mmol/L, respiratory failure cut of PaO2/FiO2 ≤200, and white cell count of ≥10 cells/liter [27]. The patient survival at one year was 100%, 79%, 64%, and 9% at score 0, 1, 2, and >2 respectively. Although, an excellent score using the clinically relevant granular data, with over 90% mortality at score >2, the score is unlikely to be useful to decide more relevant question as to whom not to transplant. The data from our study adds to this relatively small retrospective study. Further, at the other extreme with a score of 0, the survival was 100%, which seems much above the average survival of 90-95% at one year after transplantation even among patients without ACLF [24,27]. Three variables in the scoring system we developed of liver disease etiology, cardiovascular and of brain failure did not emerge significant in this study.

Although, analysis on large number of patients using the UNOS database is a strength, our study lacks validation using an external cohort of LT recipients with grade 3 ACLF at the time of LT. Further, UNOS data based adjudication may be prone to misclassification with either under or over classification to ACLF and its grade. This may therefore inflate or undermine the significance of ACLF and its grade in predicting short-term patient survival. For example, pulmonary and cardiovascular failure could have been misclassified due to unavailability of granular data in the UNOS dataset on PaO2, FiO2, blood pressure readings with number of vasopressors use. Mechanical ventilation may also have been used in patients with grade ≥3 hepatic encephalopathy to protect the airway. Similarly, vasopressor use may be for hepatorenal syndrome. Due to unavailable data in the UNOS database for sepsis, infection, white blood count, serum lactate level, [7,9,13,23,27,28] we were not able to objectively assess whether the development of ACLF in our cohort was as a result of infections or sepsis, which is known to be a major precipitant factor of ACLF.[1,29] Based on study findings in the current study, a high risk liver graft should preferably be avoided with certain donor characteristics in a patient with grade 3 ACLF. However, the decision of declining a high risk graft should factor into the patient survival with this graft versus waitlist mortality waiting for a good quality graft given that the window of opportunity short, especially during the first week after listing for patients with grade 3 ACLF.[30] It should be acknowledged that even after accounting for waitlist mortality in an intent to treat analysis, 1-yr. survival after LT among grade 3 ACLF patients is 50%.[13] Clearly, better strategies of preserving the high risk grafts should be considered and promoted with improved post-transplant outcomes. [31]

To our knowledge, this is the first study using the UNOS database with a risk score model predicting 1-yr. post-LT survival and helping to match recipient with donor graft. The findings of

our study would be useful in clinical practice and lay foundation in designing future prospective multicenter studies aiming to derive a model with improved accuracy using more granular data.

In summary, LT provides survival benefit to select patients with ACLF at the time of transplantation. However, outcomes remain suboptimal for sickest patients with ACLF grade 3 and multiple organ failure. We developed and validated a score using pre-transplant variables. Among ACLF-3 liver transplant recipients, those with high risk at the time of transplant receiving better quality graft will improve post-transplant outcomes. Prospective studies using additional characteristics are needed to derive accurate risk score model in predicting post-transplant outcomes among recipients with ACLF-3.

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**Table 1** Baseline characteristics of candidates with acute on chronic liver failure (ACLF) grade 3 at the time of liver transplantation

| | | **Whole Dataset (N=7166)** | **Derivation Dataset (N=3583)** | **Validation Dataset (N=3583)** |
|---|---|---|---|---|
| Age in years, mean (SD) | | 52.6, 10.3 | 52.7, 10.2 | 52.5, 10.3 |
| Males (%) | | 4510 (63) | 2295 (64) | 2215 (62) |
| | Caucasians | 3978 (56) | 1991 (56) | 1967 (55) |
| Race N (%) | AA | 564 (8) | 280 (9) | 284 (8) |
| | Hispanics | 2297 (32) | 1135 (32) | 1162 (32) |
| Obesity (%) | | 2983 (42) | 1475 (41) | 1508 (42) |
| MELD at LT, median (IQR) | | 36.5 (30.7-41.7) | 35.6 (30.6-41.6) | 36.6 (30.9-42.0) |
| | HCV | 2388 (33) | 1197 (33) | 1191 (33) |
| Etiology N (%) | ALD | 2148 (30) | 1050 (29) | 1098 (31) |
| | NASH | 783 (11) | 391 (11) | 392 (11) |
| Renal failure N (%) | | 6118 (85) | 3042 (85) | 3076 (86) |
| Liver failure (%) | | 6087 (85) | 3026 (84) | 3061 (85) |
| Coagulation failure (%) | | 4746 (66) | 2365 (66) | 2381 (66) |
| Brain failure (%) | | 3784 (53) | 1916 (53) | 1868 (52) |
| Pulmonary failure (%) | | 1071 (15) | 530 (15) | 541 (15) |
| Cardiovascular failure (%) | | 3427 (48) | 1738 (49) | 1689 (47) |
| Progression from listing N (%) | | 4504 (63) | 2302 (64) | 2202 (61) |

| | | | |
|---|---|---|---|
| Median (IQR) wait time | 11 (4-53) | 12 (4-56) | 11 (4-49) |
| Donor risk index, mean (SD) | 1.53, 0.32 | 1.53, 0.32 | 1.53, 0.32 |

*AA: African American, ALD: alcoholic liver disease, BMI: Body mass index, C: Caucasian, H: Hispanic, HCV: Hepatitis C virus infection, LT: Liver transplantation, MELD: Model for end-stage liver disease, NASH: Non-alcoholic steatohepatitis, SD: Standard deviation, IQR: Interquartile range.*

**Table 2** Final cox regression models including type of organ failure or number of organ failures or extra-hepatic (EH) vs. non-EH organ failure in the model.

| Variable | Model with type of organ failure | Model with number of organ failures | Model with EH organ failure |
|---|---|---|---|
| Alcohol vs. non-alcohol etiology | 0.73 (0.59-0.89), p<0.002 | 0.72 (0.59-0.89), p<0.002 | 0.71 (0.58-0.87), p<0.001 |
| Pulmonary failure at LT | 1.61 (1.29-1.99), p<0.001 | | |
| Brain failure at LT | 1.40 (1.18-1.60), p<0.001 | | |
| CV Failure at LT | 1.30 (1.09-1.56), p<0.004 | | |
| 4-6 vs. ≤3 organ failures | | 1.49 (1.26-1.77), p<0.001 | |
| EH vs. no EH organ failure | | | 1.41 (1.13-1.78) |
| Recipient age at LT (for 5 years ↑) | 1.12 (1.07-1.17), p<0.001 | 1.12 (1.07-1.17), p<0.001 | 1.11 (1.06-1.16), p<0.001 |
| Wait time in days | | 1.00 (0.99-1.00), p=0.017 | 1.00 (0.99-1.00), p=0.017 |

*LT: Liver transplantation*

**Table 3** Specific components of donor risk index and 1-yr. patient survival among liver transplant recipients with high risk score.

| | | N | 1-yr. survival | P |
|---|---|---|---|---|
| | <40 | 1284 | 81.5 | |
| Donor age in years | 40-59 | 953 | 76 | <0.001 |
| | >=60 | 253 | 66 | |
| | | | | |
| | <5 | 626 | 76.8 | |
| Cold ischemia time in hours | 5-7.9 | 1211 | 78.6 | 0.490 |
| | >=8 | 613 | 77.3 | |
| | | | | |
| | <165 | 602 | 76.7 | |
| Height in cm. | 165-179.9 | 1233 | 78.4 | 0.660 |
| | >=180 | 558 | 76.9 | |
| | | | | |
| | Anoxia | 581 | 79.4 | |
| Cause of donor death | CVA | 893 | 73.8 | 0.025 |
| | Tumor/Trauma | 925 | 80 | |
| | | | | |
| Graft type used | Whole | 2436 | 77.8 | 0.180 |
| | Split | 14 | 92.9 | |
| | | | | |
| | Local sharing | 1386 | 77.1 | |
| Source of graft | Regional sharing | 1017 | 79.6 | 0.013 |
| | National sharing | 47 | 63.8 | |
| | | | | |
| | White | 1522 | 78.2 | |
| Race | Black | 350 | 75.1 | 0.390 |
| | Other | 578 | 78.6 | |
| | | | | |
| Donor after cardiac death | No | 2387 | 80 | 0.370 |
| | Yes | 61 | 73.4 | |

## Legends to Figures

**Figure 1** Analysis of the validation dataset on **A)** calibration between observed versus expected 1-yr. patient survival among liver transplant recipients with acute on chronic liver failure grade 3 at the time of transplantation. The correlation R coefficient between observed and expected frequencies on validation dataset for patient survival at one year after LT is 0.92, and **B)** Kaplan Meier survival curves for 1-yr. patient survival based on the risk score calculated from the derivation dataset comparing low (<7.55), medium (7.55-11.57), and high risk (>11.57) categories.

**Figure 2** Patient survival rates at 1-year after liver transplantation among recipients with acute on chronic liver failure grade 3 at the time of transplant comparing good versus poor quality donor graft (cut-off donor risk index or DRI at 1.50) in the validation (A) and whole dataset (B). The data show that outcomes are better with good quality graft among transplant recipients at higher risk for patient mortality at 1-year after transplantation (risk score >11.57). The survival is similar irrespective of graft quality among those with low (risk score <7.55) or medium (7.55-11.57) risk categories.

**Figure 3** Kaplan Meier survival curves on 1-yr. patient survival among liver transplant recipients with high risk score (>11.57) comparing **A)** donor age <40 vs. 40-59 vs. ≥60 years and B) graft source local vs. regional vs. national sharing.

**Figure 4**. Kaplan Meier survival curves on 1-yr. patient survival among liver transplant recipients with high risk score (>11.57) comparing patients receiving grafts with < 15% vs. ≥15% graft macro-steatosis.