





## ORIGINAL ARTICLE

# Assessment of donor quality and risk of graft failure after liver transplantation: The ID<sup>2</sup>EAL score

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Accurate assessment of donor quality at the time of organ offer for liver transplantation candidates may be inadequately captured by the donor risk index (DRI). We sought to develop and validate a novel objective and simple model to assess donor risk using donor level variables available at the time of organ offer. We utilized national data from candidates undergoing primary LT (2013–2019) and assessed the prediction of graft failure 1 year after LT. The final components were donor Insulin-dependent diabetes mellitus, Donor type (DCD or DBD), cause of Death = CVA, serum creatinine, Age, height, and weight (length). The ID<sup>2</sup>EAL score had better discrimination than DRI using bootstrap corrected concordant index over time, especially in the current era. We explored donor-recipient matching. Relative risk of graft failure ranged from 1.15 to 3.5 based on relevant donor-recipient matching by the ID<sup>2</sup>EAL score. As an example, for certain recipients, a young DCD donor offer was preferable to an older DBD with relevant comorbidities. The ID<sup>2</sup>EAL score may serve as an important tool for patient discussion about donor risk and decisions regarding offer acceptance. In addition, the score may be preferable to succinctly capture donor risk in future organ allocation that considers continuous distribution ([www.iddealscore.com](http://www.iddealscore.com)).

## KEYWORDS

DCD, donor risk index, graft failure, graft survival, mortality, prediction model

## 1 | INTRODUCTION

Accurate assessment of donor quality at the time of organ offer for liver transplantation candidates remain suboptimal.<sup>1</sup> The development of the Donor Risk Index (DRI) was a seminal study that captured the risk

of graft failure attributed to the donor organ.<sup>2</sup> However, since its development and introduction over 15 years ago several changes have occurred. First, the DRI was developed utilizing data from the pre-Model for End-stage Liver Disease (MELD) era with lower disease severity, younger recipient population, and included patients with HCV. In the

**Abbreviations:** aHR, adjusted hazard ratio; AIC, Akaike Information Criteria; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; BSA, body surface area; CIT, cold ischemia time; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; DBD, donation after brain death; DCD, donation after cardiac death; DRI, Donor Risk Index; eGFR, estimated glomerular filtration rate; HCC, Hepatocellular Carcinoma; HCV, Hepatitis C; HR, hazard ratio; HTN, hypertension; IDDM, Insulin-Dependent Diabetes Mellitus; KDPI, Kidney Donor Profile Index; LT, Liver Transplantation; MELD, Model for End-stage Liver Disease; MELD-Na, MELD-Sodium; OPTN, Organ Procurement and Transplantation Network; RCS, restricted cubic spline; SRTR, Scientific Registry of Transplant Recipients; TRIPOD, Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis.

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current era, recipients are sicker, older, and have more comorbidities.<sup>3</sup> In addition, the risk of graft failure associated with hepatitis C (HCV) has decreased especially in the direct-acting antiviral (DAA) era; hence, its historical statistical weight in predictive modeling may no longer be applicable.<sup>4-6</sup> Second, there has also been a change in donor acceptance patterns over time with an increase in the use of donation after cardiac death (DCD) organs as well as older donors.<sup>4,5,7</sup> Surgical expertise and ability to handle sicker and older organs has improved which may mitigate the risk attributed to historical factors.<sup>7</sup> In addition, decisions in organ acceptance for donation after brain death (DBD) are likely different from those taken for DCD. Third, there has been a change in organ allocation policy with the introduction of acuity circles.<sup>7-9</sup> Specifically, the impact of total travel time (with cold ischemia time [CIT] as a surrogate) is further emphasized.<sup>10,11</sup> Future updates to organ distribution are being considered (e.g., continuous distribution), whereby accurate assessment of risk attributed to decision regarding donor organ may play a larger role.<sup>9,12,13</sup> In total, changes in donor and recipient characteristics and practice patterns sets up a need to reevaluate aspects of donor risk assessment.

Reassessment of the composite impact of donor factors may be helpful for several reasons. A new model to assess donor risk at time of offer may be helpful to identify the maximum tolerated CIT for a given organ to a potential recipient, especially if there is an ability to vary the purported impact of various factors at the same time (e.g., age and other surrogates of donor quality). Second, it may allow for granular discussion with patients about the predicted risk of graft failure. Specifically, for low MELD-Sodium (MELD-Na) patients it may allow for discussion about living donation after placing donor factors and association with long-term morbidity and mortality in context. Finally, an updated model may help play a role in donor-recipient matching when confronted with multiple offers for a given patient.

We hypothesized that the performance of DRI has changed over time. With that in mind, we sought to develop and validate a novel objective and simplified model to assess donor risk, the ID<sup>2</sup>EAL score (described below), using donor level variables available at the time of organ offer. In addition, we explored a potential role for the ID<sup>2</sup>EAL score in clinically relevant and representative situations of donor-recipient matching.

## 2 | METHODS

The Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis (TRIPOD) guidance statement was used as a guide to follow standard tools in prediction model development and validation.<sup>14</sup>

### 2.1 | Case ascertainment

We utilized data submitted to the Scientific Registry of Transplant Recipients (SRTR) on all adult (age ≥ 18 years) patients listed and

undergoing primary liver transplantation (LT) from July 1, 2013, and December 31, 2019. This allowed for at least 1 year follow-up for outcomes after LT through 2020. We excluded patients that were listed for re-transplantation, partial graft, multiple organ transplantation, or those that were status 1 and/or listed for acute liver failure as decision regarding organ type may differ for these indications. Registrants with HCV diagnosis were excluded given that mortality attributed to HCV in the study period may not reflect current patterns with widespread use of DAA.<sup>6,15</sup> As a sensitivity analysis, we examined the derived model in patients transplanted for HCV and performance was similar. Candidates with exception points were included but calculated/biologic MELD was used. Figure S1 shows patient flow.

### 2.2 | Data source

The SRTR data system includes data on all donors, waitlisted candidates, and transplant recipients in the United States, submitted by the members of the Organ Procurement and Transplantation Network (OPTN), and has been described elsewhere.<sup>16</sup> The Health Resources and Services Administration, US Department of Health and Human Services, provides oversight of the activities of the OPTN and SRTR contractors. The data set provided by the SRTR includes a comprehensive array of variables about the transplant, recipient, and donor.

### 2.3 | Statistical analysis

#### 2.3.1 | Outcome

The primary outcome was graft failure 1 year after LT. Graft failure was defined as patient death, re-transplantation, or relisting for re-transplantation. Patients were followed from the time of transplant until the earliest of graft failure, death, loss to follow-up, or the conclusion of the observation period.

### 2.4 | Model development

#### 2.4.1 | Variables of interest

The primary variables of interest were donor factors available at the time of LT. In addition, a priori we considered potential surrogates of decision making<sup>1</sup>: type of organ (DBD vs DCD),<sup>2</sup> surrogates for size mismatch or organ size (body surface area [BSA], height, and weight), and<sup>3</sup> putative surrogates of organ quality (body mass index [BMI], steatosis, donor insulin-dependent diabetes mellitus, donor kidney function-serum creatinine or estimated glomerular filtration rate [eGFR], and advanced age [donor age, donor cause of death]).<sup>17,18</sup> eGFR was estimated using the current Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula with and without

race.<sup>19</sup> Cold ischemia time was examined as a known determinant as well as a potential surrogate for travel time.<sup>18</sup> We did not consider split organs and re-transplantation (given that decision making may be different) or donor race given the lack of biological plausibility.<sup>20</sup> Factors considered but did not appear to be significantly associated with the outcome either by clinical relevance, visual inspection of spline transformation or on adjusted analysis included: donor aspartate aminotransferase (AST), alanine aminotransferase (ALT), bilirubin, steatosis, BMI, hypertension (HTN), sodium, and donor vasopressor use.

#### Missing data

Most of the donor variables, including donor demographics, height, and weight, donor sodium, donor diabetes (missing 1.5%), and donor cause of death, had no or very few missing values. Only 0.2% of patients in the study cohort had missing cold ischemia time. Donor macro steatosis was missing in 63.3% of cases and was not included in multivariate analyses. In sensitivity analysis, a model with reported steatosis did not improve prediction. Because the sample size was large enough for adequate power and the percentage of missing data was negligible, we conducted a complete case analysis and imputation was not needed.

#### Linearity and interactions

Linear assumption was met for all variables using linearity Wald tests via restricted cubic spline (RCS) transformations except for donor BSA and weight ( $p = .01$ ). We analyzed donor height, donor BMI, and donor BSA separately in alternative models because of collinearity, and we compared the models using the Akaike Information Criteria (AIC). Donor height and donor BSA had a similar association with outcome. For ease of use, we considered height and weight instead of BSA. Donor creatinine had a similar association with outcome as compared to eGFR by CKD EPI with and without race. Hence for ease of application, we used donor creatinine. There was no collinearity between IDDM and eGFR.

#### Final model

The prediction model was built using the Cox proportional hazard regression and backward selection on the entire data set and then resampled using 300 bootstrapping for internal validation to evaluate the performance and quantify the optimism of the developed model. A significance level of a factor to be kept in the model was set to 0.1.

#### Proportional hazard assumption

We tested the proportional hazard assumption, verifying the pattern of the scaled Schoenfeld residuals against the ranked time variable. We did not observe any trend against time and no major violations. We tested the validity of the proportional hazard assumption for each covariate and globally. The global test of proportional hazard was not statistically significant ( $p = .06$ ) indicating that the proportionality of hazards was met at significance level  $\alpha = 0.05$ .

#### ID<sup>2</sup>EAL score

The final components were donor Insulin-dependent diabetes mellitus, Donor type (DCD or DBD), cause of Death = CVA, serum creatinine, Age, height, and weight (length) (ID<sup>2</sup>EAL score). To explore how donor factors changed in subgroups of biochemical MELD-Na scores we tested pre-specified interactions within MELD-Na strata. We considered a model containing a second-order interaction for the triplet of factors, as well as all first-order interactions. The interaction effects were not significant. The final model was adjusted for recipient MELD-Na, recipient age, and cold ischemia time considered as continuous variable.

#### Validation

To internally validate the Cox PH model performance and correct overfitting or optimism we used bootstrap resampling. The final prediction was evaluated for its ability to discriminate subjects with high and low scores. Calibration plots of the observed versus predicted probability plots were used to internally validate the accuracy of predictions.

## 2.5 | Performance

### 2.5.1 | Discrimination and calibration

Bootstrap with 300 resamples was used to validate the ID<sup>2</sup>EAL model. The bootstrap corrected concordant index over time (time-dependent AUC) was used to assess discrimination of the ID<sup>2</sup>EAL score. We used calibration to evaluate the observed and predicted estimated graft survival probability within 1-year post-LT. We calculated an optimism-corrected calibration slope. We compared the mean absolute error in predictions and the 0.9 quantiles of the absolute error, where error refers to the difference between the predicted values and the corresponding bias-corrected calibrated values.

We compared to DRI by considering a model that adjusted for the same variables used in the ID<sup>2</sup>EAL score and included DRI as a predictor and tested for differences in model performance.

## 2.6 | Donor-recipient matching

Given the importance of donor-recipient matching and the need to identify the role of the proposed model for practical and relevant clinical decision making, we examined several representative scenarios. First, we examined rates of graft failure within 1 year by MELD-Na (<15, 15–28, 29–32, 33–36, and 37+) and CIT. We also created a “heatmap” to visually assess the maximally tolerated CIT for pertinent scenarios. We also examined warm ischemia time as an exploratory analysis, but data was only available for 64.5%. We also derived models that included ratios of donor and recipient height and weight ratio or body surface area. Donor and recipient gender mismatch was not significant when added to ID<sup>2</sup>EAL model

or in univariate models. Further, in the model with D/R matching by height/weight or BSA, gender mismatch was not significant.

All statistical analyses utilized R version R4.1.3 (R Foundation for Statistical Computing, Vienna, Austria). Statistical significance was set at  $p < .05$ . The study was approved by the Baylor institutional IRB.

### 3 | RESULTS

#### 3.1 | Cohort characteristics

The study population consisted of 29 127 adult recipients of primary deceased donor between July 1, 2013, and December 31, 2019 (Table 1). The median age was 58 (IQR 50–64), 34.3% females, with a median height (cm) of 173 (IQR 165–180), a median weight (kg) of 84 (IQR, 72–99) a median MELD-Na 22 (IQR 14–32) at time of LT. The median donor age was 43 years (IQR 29–56), CIT was 5.73 hours (IQR 4.52–7.12), and 6.2% insulin-dependent diabetes mellitus (IDDM). Degree of macrovesicular steatosis fat was only available in 39.5% of donors. Figure 1 explores the adjusted relationship between each donor variable used in the ID<sup>2</sup>EAL score and graft failure within 1 year.

#### 3.2 | ID<sup>2</sup>EAL score

Table 2 shows the adjusted analysis of variables included in the ID<sup>2</sup>EAL score. Recipients of DCD grafts were more than 1.6 times likely to lose their grafts within 1-year post-LT (adjusted HR [aHR] = 1.62, 95% CI 1.42–1.86). Receiving donors with insulin-dependent diabetes was associated with an increased risk of graft failure within 1-year post-LT (aHR = 1.26, 95% CI 1.09–1.46). A 10 cm decrease in donor height resulted in an increase in the risk of graft failure by 8% (aHR = 1.08, 95% CI 1.05–1.11). The relationship for weight (kg) was not linear and best modeled by restricted cubic spline. Across all factors, the adjusted relative hazard was higher among DCD organs (Figure S2) Table 3 shows the final equation for the ID<sup>2</sup>EAL score.

Figure 2 shows the probability of graft survival with 1 year ( $p < .01$ ) by quartiles of ID<sup>2</sup>EAL and Figure 3 shows the risk score models with cold ischemia time (Figure 3A) and donor and recipient height and weight (Figure 3B). Risk stratification by ID<sup>2</sup>EAL score had improved discrimination compared to the adjusted DRI in the current era (Figure 3C). Stratification was more evident in earlier eras by DRI but less so in 2017–2019 (Figure S3). In sensitivity analysis, performance was similar when of ID<sup>2</sup>EAL score was applied to patients with HCV (Figure S4).

Discrimination was improved by ID<sup>2</sup>EAL score compared to the adjusted DRI model ( $p < .01$ ; Figure S5). The bootstrap calibration metrics for the ID<sup>2</sup>EAL model are shown in Figure S6. However, the addition of ratios of D/R height and weight or BSA to the model instead of donor height and weight did not improve model performance with regards to discrimination or calibration.

TABLE 1 Donor and recipient characteristics, January 7, 2013, to December 31, 2019

| N = 29 127                         |                      |
|------------------------------------|----------------------|
| <b>Recipient characteristics</b>   |                      |
| Age at TX                          | 58.0 [50.0;64.0]     |
| Female                             | 34.3%                |
| Weight (Kg)                        | 84.4 [71.7, 98.9]    |
| Height (cm)                        | 173 [165;180]        |
| MELD-NA                            | 22.0 [14.0;32.0]     |
| MELD-NA at LT                      |                      |
| <15                                | 25.9%                |
| 15–28                              | 38.4%                |
| 29–32                              | 8.0%                 |
| 33–36                              | 6.8%                 |
| 37+                                | 20.9%                |
| Cold ischemia time (h)             | 5.73 [4.52;7.12]     |
| <b>Donor characteristics</b>       |                      |
| Donor COD:                         |                      |
| Anoxia                             | 38.4%                |
| CVA                                | 31.4%                |
| Other                              | 2.4%                 |
| Trauma                             | 27.7%                |
| DCD                                | 7.9%                 |
| Donor age                          | 43.0 [29.0;56.0]     |
| Donor female (%)                   | 40.4%                |
| Donor/s height (cm)                | 172 [165;178]        |
| Donor/s weight (kg)                | 80.7 [68.4;95.3]     |
| Donor creatinine                   | 1.04 [1.00;1.53]     |
| eGFR                               | 75.8<br>(38.8;108.5) |
| eGFR <45 ml/min                    | 28.8%                |
| % Micro vesicular fat (n = 12 151) | 5.00 [0.00;15.0]     |
| Insulin-dependent diabetes         | 6.2%                 |
| Hypertension                       | 38.0%                |
| Hypernatremia                      | 7.7%                 |

#### 3.3 | Representative scenarios

We further explored different scenarios that may arise at the time of offer for a given MELD-Na score and relative to cold ischemia time. The reference donor was age 43 years, 80.7 kg and a high of 172 (cm), DBD, no-CVA cause of death and without insulin-dependent diabetes, Figure 4A–F shows examples of various donor characteristics described from optimal to suboptimal based on a reference donor. As seen across Panels A–C, adjusted relative hazard increases as CIT increases for the various donor categories. A similar pattern is seen for DCD (panel D–F). However, as compared for the same donor category for DBD, the adjusted relative hazard is higher for DCD (e.g., A vs. D). Further progression across different donor categories (D–F) is also higher for DCD across all categories. Figure 5

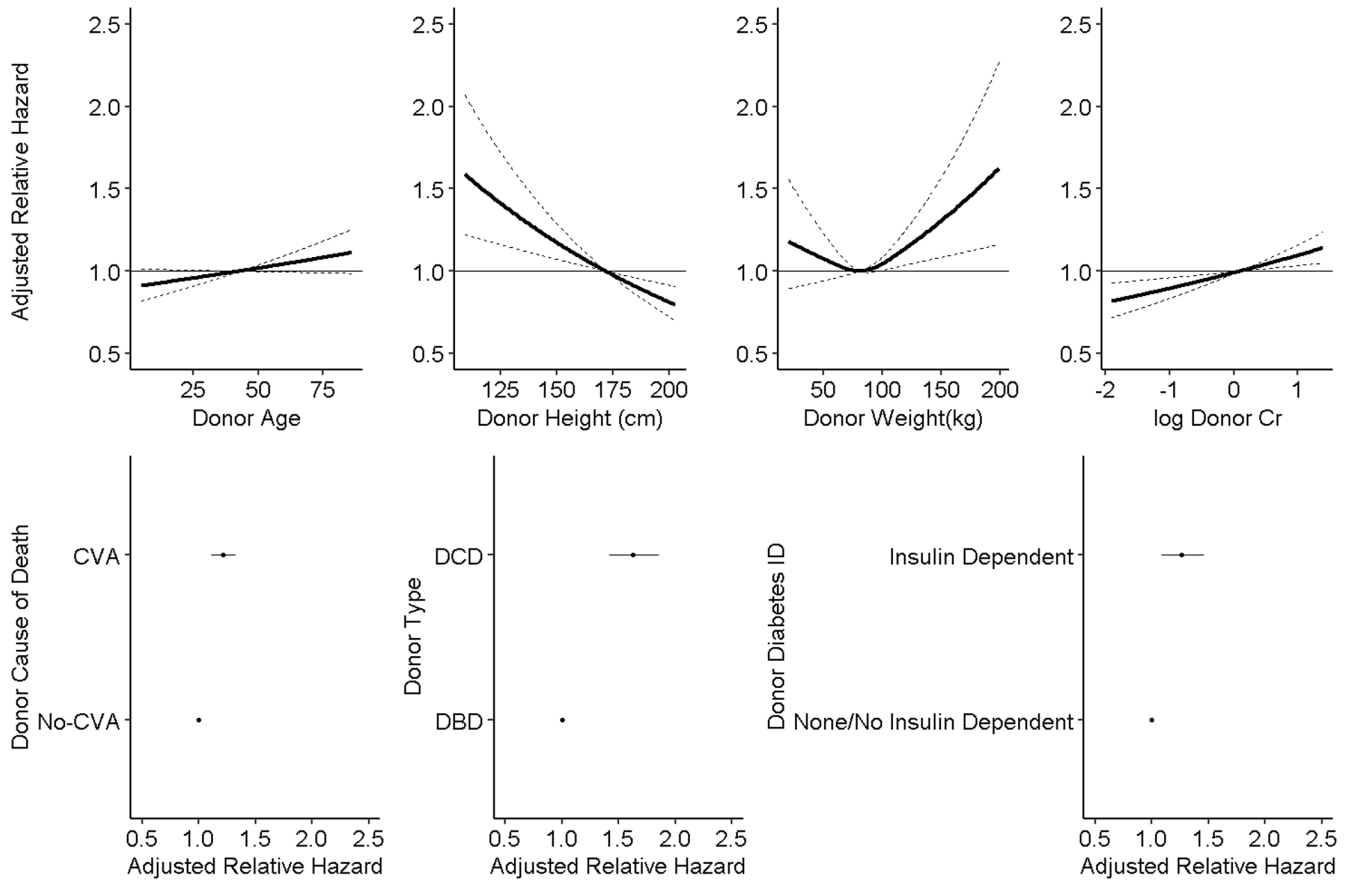


FIGURE 1 Relation of each donor variable used in the ID<sup>2</sup>EAL score and the adjusted relative hazard of graft failure within 1 year.

TABLE 2 Association of donor factors (ID<sup>2</sup>EAL score) and graft failure within 1 year after liver transplantation

| Donor factor                     | Estimated $\beta$ (SE $\beta$ ) | aHR    | 95% CI       | p-value |
|----------------------------------|---------------------------------|--------|--------------|---------|
| Insulin-dependent diabetes       | 0.230 (0.076)                   | 1.26   | 1.086, 1.460 | .003    |
| None/No insulin-dependent        | Reference                       |        |              |         |
| Donation after circulatory death | 0.485 (0.069)                   | 1.62   | 1.418, 1.861 |         |
| DBD                              | Reference                       |        |              |         |
| Cause of death-CVA               | 0.193 (0.046)                   | 1.21   | 1.108, 1.328 | <.001   |
| Non-CVA                          | Reference                       |        |              |         |
| Creatinine (log)                 | 0.101 (0.033)                   | 1.11   | 1.038, 1.180 | .002    |
| Age (10 years increase)          | 0.002 (0.001)                   | 1.025  | 1.010, 1.040 | .083    |
| Height (10 cm decrease)          | -0.074 (0.002)                  | 1.0768 | 1.054, 1.11  | <.001   |
| Donor weight (kg) <sup>a</sup>   |                                 |        |              | .022    |

Abbreviations: aHR, adjusted hazard ratio; CI, confidence interval; CVA, cerebrovascular accident.

<sup>a</sup>Donor weight is modeled as restricted cubic spline with 3 knots. Results of multivariate Cox proportional hazards model are shown adjusted for CIT, MELD-Na, and recipient age.

TABLE 3 ID<sup>2</sup>EAL risk score equation (<http://www.iddealscore.com>)

The ID<sup>2</sup>EAL risk score is an estimate of the relative risk of post-transplant graft failure for an adult recipient from a cadaveric donor, compared to a reference donor:

Reference donor: DBD donor, 43 year old; cause of death = No-CVA, No insulin-dependent, Cr = 1.1, height = 172 cm, weight = 80.7 kg

Reference CIT: 5.7 h Reference Recipient: MELD-NA = 22, age = 58

$Prob\{T \geq t\} = S_0(t)e^{X\beta}$ , were

$\hat{X}\beta =$

- 0.2685732+
- 0.002460574 × (Donor Age)
- +0.19303855 [CVA].
- +0.48533316 [DCD].
- +0.23100407 [Insulin-Dependent].
- +0.10148276 × ln (Donor Cr).
- 0.0073513206 × (Donor height (cm)).
- 0.0031065705 × (Donor weight (kg)).
- + 2.235278 × 10<sup>-6</sup> (Donor weight (kg) - 59)<sub>+</sub><sup>3</sup>.
- 3.8308547 × 10<sup>-6</sup> (Donor weight (kg) - 80.7)<sub>+</sub><sup>3</sup>.
- +1.59557767 × 10<sup>-6</sup> (Donor weight (kg) - 111.1)<sub>+</sub><sup>3</sup>.

If considering donor-recipient matching

- +0.052762643 × CIT +
- +0.011099098 × MELD-NA +
- 4.097282 × 10<sup>-5</sup> (MELD NA - 21)<sub>+</sub><sup>3</sup>
- 0.00014750215 × (MELD NA - 34)<sub>+</sub><sup>3</sup>
- +0.00010652933 × (MELD NA - 39)<sub>+</sub><sup>3</sup>
- +0.00819818 × (Recipient Age at Tx) +
- 1.4778952 × 10<sup>-5</sup> (Recipient Age at Tx - 40)<sub>+</sub><sup>3</sup>
- 4.1381067 × 10<sup>-5</sup> (Recipient Age at Tx - 58)<sub>+</sub><sup>3</sup>
- +2.6602114 × 10<sup>-5</sup> (Recipient Age at Tx - 68)<sub>+</sub><sup>3</sup>

where:

[c] = 1 if subject is in group c, 0 otherwise;

(x)<sub>+</sub> = x if x > 0, 0 otherwise

$$ID^2EAL\ Score = \exp(\hat{X}\beta)$$

R function to calculate score available upon request

shows a potential application for a given offer. Depending on the type of offer, the heat map offers guidance of the risk of mortality given a recipient MELD as well as the range of cold ischemia time. Analogous heat map is created for warm ischemia time, noting a large amount of missing data (Figure S7).

## 4 | DISCUSSION

Assessment of risk attributed to donor organ in patients undergoing liver transplantation is important, albeit difficult. In our study, we propose that the ID<sup>2</sup>EAL score captures relevant aspects of donor quality in the current era ([www.iddealscore.com](http://www.iddealscore.com)). There are several notable findings.

First, outcomes in the current era after LT are excellent and likely attributed to better multidisciplinary assessment and surgical management of donor-related issues. Despite risk stratification (by

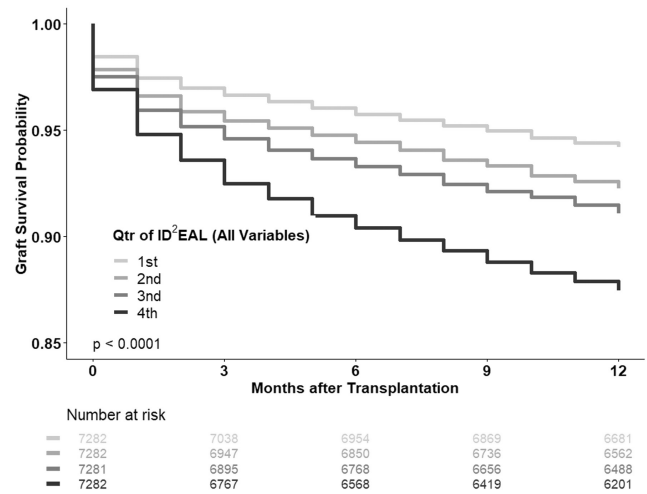


FIGURE 2 Graft survival within 1 year as assessed by the ID<sup>2</sup>EAL score.

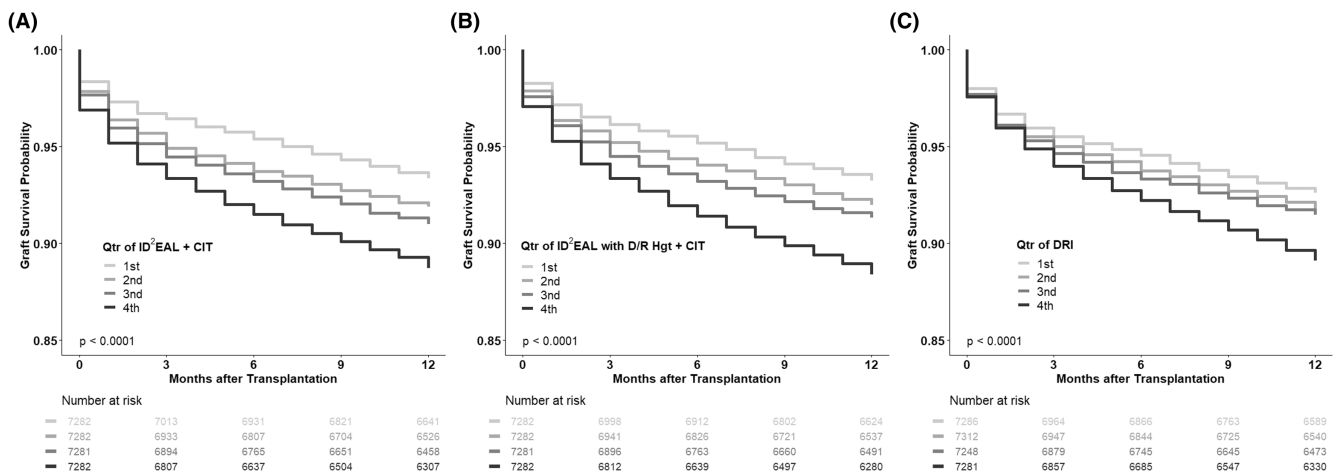
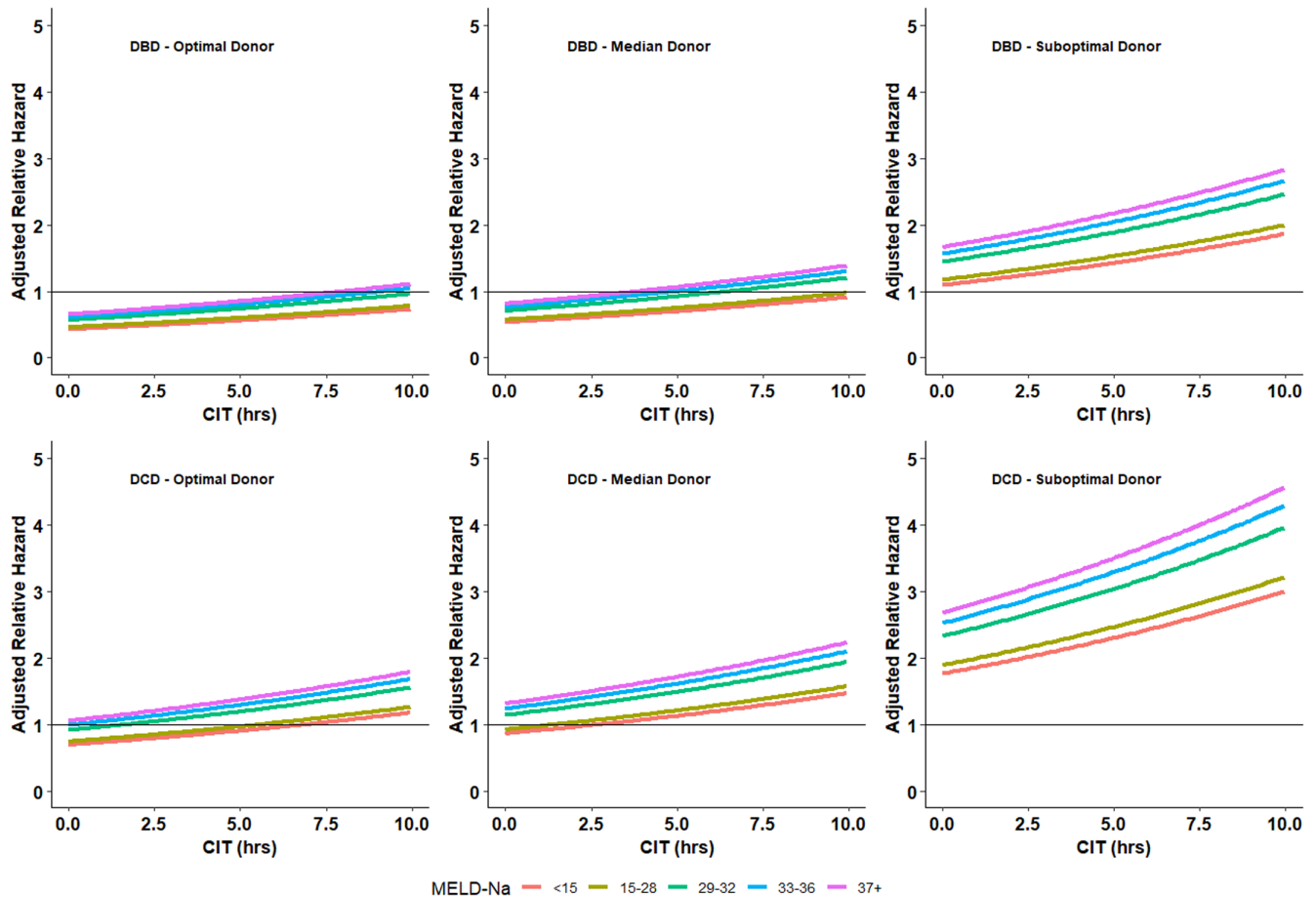


FIGURE 3 Graft survival within 1 year as assessed by the ID<sup>2</sup>EAL score with CIT (A), CIT plus D/R height (B), and donor risk index (C).

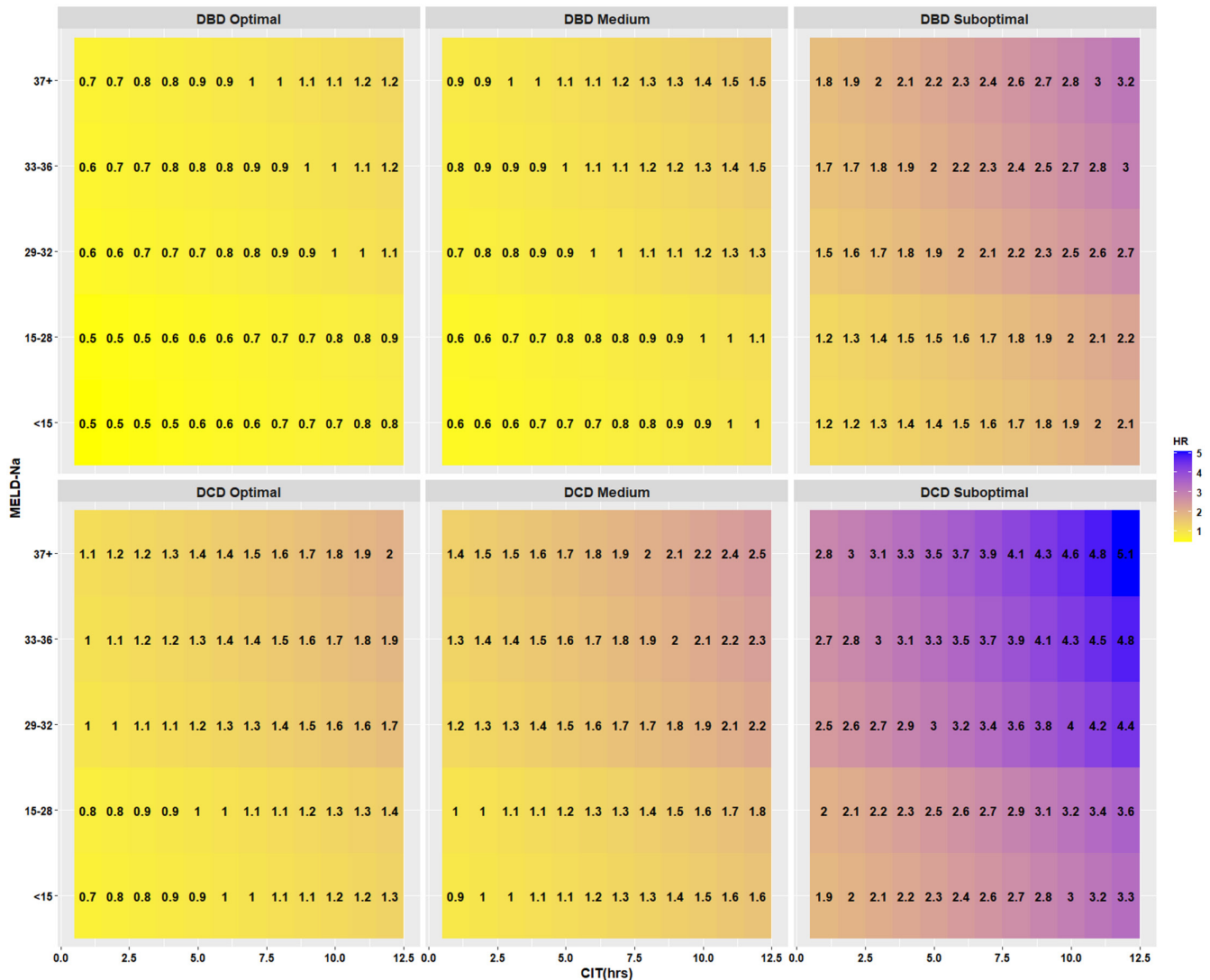


**FIGURE 4** Exploring the relation between adjusted relative hazard of graft failure by ID<sup>2</sup>EAL score given cold ischemia time, DBD and DCD status, and MELD-Na score. OPTIMAL: Donor Age = 20 years; Diabetes = "None/No Insulin-Dependent," Cr = 1.1; Donor weight = 81 kg; Donor height = 190 cm; Donor Cause of Death = "No-CVA." MEDIUM: Donor Age = 45 years; Diabetes = "None/No Insulin-Dependent"; Cr = 1.0 Donor weight = 100 kg; Donor height = 172 cm; Donor Cause of Death = "No-CVA." SUBOPTIMAL: Donor Age = 61 years; Diabetes = "Insulin-Dependent"; Cr = 3.56; Donor Weight = 130 kg; Donor Height = 172 cm; Donor Cause of Death = "CVA." [Color figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]

almost any post-transplant model), the absolute difference in donor risk between the "optimal" donor quality and "suboptimal" donor organ is likely less than 12% within 1 year of transplant. However, larger differences exist in the context of donor-recipient matching. Second, factors that were significant in the past (in attributable risk) are no longer major drivers.<sup>21</sup> Third, donor-related factors that drive outcomes in the current era (ID<sup>2</sup>EAL score) reflect our increasing use of DCD organs, donor size (height and weight or body surface area) and novel and established surrogates of organ quality (e.g. donor creatinine, age, cause of death = CVA, insulin-dependent diabetes). Fourth, the ID<sup>2</sup>EAL score may serve as an important bedside tool for patient discussion about donor risk and decisions regarding offer acceptance that take into account donor-recipient matching.<sup>22</sup>

The ID<sup>2</sup>EAL score may integrate with our clinical decision-making in the following manner. First, it may allow us to have a frank discussion with our patients about the relative risk of various aspects of organ acceptance for a patient within a given MELD-Na stratum. It also highlights the tradeoffs in organ acceptance of balancing patients' clinical condition and possible future offers or weighing the risks of a particular deceased donor offer with those of a living donor

liver transplant. The model might be informative to examine the risk of not taking an organ and subsequent risk of waitlist mortality versus accepting different types of extended criteria organs. Patients want to be involved in the decision-making process, and an objective tool that encapsulates donor risk is highly relevant.<sup>23</sup> Such discussions are relevant for encouraging living donor liver transplantation in a majority of registrants. Second, it may serve as a practical tool at the time of organ offer to assess the relative merit of potential matching. As an example, representative scenarios show that certain donor combinations may not be tolerated across the entire range of MELD-Na scores.<sup>24,25</sup> On the other hand, in organs with suboptimal donor combinations, only minimal increases in cold ischemia time or distance may be tolerated especially given a certain MELD-Na score. Third, the ID<sup>2</sup>EAL score may serve as an important component of future changes in organ allocation and distribution. As an example, the kidney donor profile index (KDPI), a surrogate of kidney donor quality plays an important role in organ distribution for kidney transplantation.<sup>26</sup> In addition, a framework for organ acceptance and distribution (continuous distribution) that goes beyond the singular focus on medical urgency is being considered for all



**FIGURE 5** Exploring relation between adjusted relative hazard of graft failure by ID<sup>2</sup>EAL score given cold ischemia time and MELD-Na score using a heat map. [Color figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]

organ transplants.<sup>13,27,28</sup> One may envision that along with medical urgency as captured by MELD-Na score, additional factors such as organ quality (potentially captured by the ID<sup>2</sup>EAL score) may play a role in either organ acceptance or relative ranking of priority given two candidates or two potential offers.

The strength of our study is methodical consideration of model development and validation. We sought to identify a focused set of variables based on clinical relevance that impact post-LT outcomes. We used a relevant comparator (DRI) that has served as an effective benchmark of donor quality across various studies. Risk stratification by quintiles was better for ID<sup>2</sup>EAL as compared to DRI. Our methodology captures the essence of decision-making when multiple factors, in addition to donor quality, are considered. In addition, our model may have clinical utility in being an effective tie breaker in consideration of candidates with the same MELD score being offered multiple offers.<sup>27</sup>

Our study has limitations. Donor factors are only one part of the decision-making and surgeon level/program-based decisions

to accept offers cannot be modeled. In contrast to kidney transplant whereby most recipients are relatively stable, there is wide variation in recipient characteristics for potential liver transplant. At high MELD scores, mortality post-LT may be driven predominantly by recipient rather than donor factors. However, we show several donor-recipient scenarios by MELD, CIT as well as recipient characteristics to describe its proposed application. Missing data did not allow us to comprehensively study the impact of steatosis. However, a model with steatosis did not improve prediction. In addition, there is often a disconnect between recorded steatosis and the transplant team's assessment of steatosis. Decisions for organ acceptance may vary for DBD vs DCD organs. We captured this by showcasing relative attribution of other factors in the model stratified by DCD or DBD status. Finally, our study does not capture all recipient, transplant, and donor-related factors either before or after transplant that may influence outcomes. However, our intent was to develop a model that relies on information readily available to have an informed discussion with patients at the time of offer to augment



clinical decision-making. We did not compare our model to other alternatives such as UK-DCD, balance of risk (BAR) score or survival outcomes following liver transplantation (SOFT) score since these models include both donor and recipient factors not readily available at time of decision making.<sup>29</sup> For example, the UK-DCD model assigns the highest statistical weight to warm ischemia time and retransplantation candidates, obviating their role as being effective comparators in this current analysis. Similarly, the SOFT score uses 18 donor and recipient risk factors with the most significant risk factors being previous transplants, warm ischemia time, and the need for life support.<sup>30</sup> The BAR score does consider donor-recipient matching, but its definition of futility is applicable to only 3% of the population.<sup>29</sup> Future studies will need to examine the role of a donor model combined with recently published models assessing recipient risk.<sup>6,30,31</sup> However, we explored the potential contribution of warm ischemia time only as an exploratory analysis, given a large amount of missing data.

In summary, the DRI helped the transplant community capture the impact of donor factors in transplant decisions. The ID<sup>2</sup>EAL score builds on this concept and may more accurately capture risk attributed to donor factors in the current era as well as serve as an important tool in taking care of our patients with liver disease and also serve as stewards of a precious resource. Further studies are encouraged to further explore center variation in donor-recipient matching as well as its role in future continuous distribution paradigms.

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## DATA AVAILABILITY STATEMENT

Available upon request.

## DISCLOSURE

The authors of this manuscript have no conflicts of interest to disclose as described by the *American Journal of Transplantation*. Authors had access to all the study data, take responsibility for the accuracy of the analysis, and had authority over manuscript preparation and the decision to submit the manuscript for publication. All authors approved the manuscript. The data reported here have been supplied by the Hennepin Healthcare Research Institute (HHRI) as the contractor for the Scientific Registry of Transplant Recipients (SRTR). The interpretation and reporting of these data are the responsibility of the author(s) and in no way should be seen as an official policy of or interpretation by the SRTR or the US government.

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## SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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