COMBINING DONOR AND RECIPIENT AGE WITH PREOPERATIVE MELD AND UKELD SCORES FOR PREDICTING SURVIVAL AFTER LIVER TRANSPLANTATION

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COMBINING DONOR AND RECIPIENT AGE WITH PREOPERATIVE MELD AND UKELD SCORES FOR PREDICTING SURVIVAL AFTER LIVER TRANSPLANTATION

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ABSTRACT

Objectives: MELD, UKELD and D-MELD (donor age x MELD) have been assessed as scores for predicting survival after orthotopic liver transplantation (OLT), but with mediocre results. We introduced new indices based on preoperative MELD and UKELD scores, assessed their predictive ability concerning post-OLT survival, and compared it with that of the pre-existing scores.

Methods: We included 1017 OLTs from deceased donors that were performed in our department between 2008 (the year UKELD was introduced) and 2019. Data were collected about donor and recipient characteristics (including MELD and UKELD scores), and transplant characteristics and outcomes. The following scores were calculated: D-MELD, D-UKELD (donor age x UKELD), DR-MELD [(donor age+recipient age)xMELD], DR-UKELD [(donor age+recipient age)xUKELD].

Results: No score had predictive value concerning graft survival. Regarding patient survival, DR-MELD and DR-UKELD provided the best results, but with a low accuracy. The highest accuracy was observed at 1 year post OLT (DR-MELD: AUC: 0.598, 95%CI: 0.529-0.667, DR-UKELD: AUC: 0.609, 95%CI: 0.549-0.67). The addition of donor and recipient age improved the predictive ability of MELD and UKELD scores regarding patient survival significantly, but the addition of donor age alone did not. Based on ROC curves for 1-year mortality, the optimal cut-off points were DR-MELD>2345 and DR-UKELD>5908. Recipients with DR-MELD>2345 had worse patient survival within the first year ($p<0.001$), which remained in the multivariable analysis (HR: 2.263, 95%CI: 1.257-4.074, $p=0.007$). Recipients with DR-UKELD>5908 had worse patient survival within the first year ($p=0.002$), but this did not remain in the multivariable analysis (HR: 1.588, 95%CI: 0.966-2.611, $p=0.068$).

Conclusions: DR-MELD and DR-UKELD scores provide the best, albeit mediocre, predictive ability among the six tested models, especially at 1 year post OLT, but only regarding patient survival and not graft survival. DR-MELD>2345 can be considered an additional independent risk factor for worse recipient survival within the first postoperative year.

Key words: liver transplant, age, MELD, UKELD, survival

INTRODUCTION

Malinchoc et al. introduced the Model for End-Stage Liver Disease (MELD) score in 2000 as a tool to predict 3-month survival of cirrhotic patients undergoing transjugular intrahepatic portosystemic shunts (TIPS), based on serum bilirubin, the international normalized ratio for prothrombin time (INR) and serum creatinine.[1] Kamath et al. in 2001[2] and Wiesner et al. in 2003[3] demonstrated that MELD score can also be used to predict 3-month survival of cirrhotic patients with end-stage liver disease waiting for orthotopic liver transplantation (OLT) and could be used to allocate organs to those most in need of transplant. Neuberger et al. introduced the United Kingdom Model for End-Stage Liver Disease (UKELD) score in 2008 as a new tool for predicting mortality of cirrhotic patient on the waiting list for OLT, based on serum bilirubin, INR, serum creatinine and serum sodium.[4] According to Barber et al., UKELD score is superior to MELD score in predicting of 3-month and 1-year mortality of cirrhotic patients waiting to be transplanted.[5]

MELD and UKELD scores have been used to predict graft and recipient survival post OLT, but the accuracy is low with an area under the sensitivity/specificity curve (AUC) being less than 0.7.[6-12] Halldorson et al. described in 2009 the D-MELD score, which is the product of donor age and preoperative MELD score, trying to combine a major factor of liver graft quality, namely the donor age, with the severity of recipient's liver failure, as depicted by MELD score,[13] but AUC values remained less than 0.7[6-9,14] and comparative studies showed no significant difference between MELD, UKELD and D-MELD scores.[7,9-11]

Our aim was to introduce new indices combining preoperative MELD or UKELD scores with donor and recipient age. We assessed their predictive ability in regards to graft and patient survival post OLT, along with that of the already existing

aforementioned scores. In particular, we introduced D-UKELD score (the product of donor age and UKELD score), DR-MELD score (the product of MELD score and the sum of donor and recipient age) and DR-UKELD score (the product of UKELD score and the sum of donor and recipient age). We also assessed if the addition of donor age or the sum of donor and recipient age to MELD or UKELD score improves their prognostic ability, and tried to identify the optimal cut-off points of the scores providing the best results.

PATIENTS AND METHODS

Patients

We retrospectively reviewed our prospectively maintained database in November 2019 for OLTs performed in our department between January 2008 and November 2019. This is the source of the validated data for the unit provided to the National Health Service Blood and Transplant (NHSBT) organisation. We chose January 2008 as the beginning of our study period, because UKELD score was introduced in that year. One thousand and thirty-eight liver-only transplants from deceased donors were performed over this period, 870 (83.8%) from donation after brain death (DBD) and 168 (16.2%) from donation after circulatory death (DCD). We included 1017 OLTs [849 (83.5%) DBD and 168 (16.5%) DCD] in our analysis, after excluding 21 cases for which we did not have both preoperative MELD and UKELD scores available. Table 1 summarizes patient and transplant characteristics.

Data were collected concerning the following parameters:

1. Donor characteristics: age, gender, donor type (DBD or DCD), graft type (whole or split), liver steatosis,

2. Recipient characteristics: age, gender, ethnicity, body mass index (BMI), urgency for OLT (urgent or elective), indication for OLT, previous OLT, preoperative MELD score, preoperative UKELD score,

3. Transplant technique (caval replacement or piggyback),

4. Cold ischaemia time (CIT) (time between aortic cross-clamp with initiation of donor's cold perfusion and liver reperfusion with recipient's blood),

5. Transplant outcomes: graft survival, patient survival.

MELD score was calculated as follows: MELD = 9.57 x ln[serum creatinine (mg/dl)] + 3.78 x ln[serum bilirubin (mg/dl)] + 11.2 x ln[INR] + 6.43 x [0 if cholestatic or alcoholic aetiology, 1 otherwise].[1-3] D-MELD was estimated as the product of donor age and preoperative MELD score [D-MELD = (donor age) x MELD].[13] DR-MELD was estimated as the product of preoperative MELD score and the sum of donor and recipient age [DR-MELD = (donor age + recipient age) x MELD].

UKELD was calculated as follows: UKELD = 5.395 x ln[INR] + 1.485 x ln[serum creatinine (μmol/L)] + 3.13 x ln[serum bilirubin (μmol/L)] – 81.565 x ln[serum sodium (mmol/L)] + 435.[4,5] D-UKELD score was estimated as the product of donor age and preoperative UKELD score [D-UKELD = (donor age) x UKELD]. DR-UKELD was estimated as the product of preoperative UKELD score and the sum of donor and recipient age [DR-UKELD = (donor age + recipient age) x UKELD].

Our study conforms to the 2000 Declaration of Helsinki, the 2008 Declaration of Istanbul and the guidelines of the ethics committee of our institution.

Statistical analysis

Time-dependent receiver operating characteristic (ROC) analysis was performed to assess the ability of MELD, D-MELD, DR-MELD, UKELD, D-UKELD and DR-UKELD scores to predict graft loss and death across time, using the "timeROC" R package. The AUC was calculated at three different time points: 1 year, 3 years and 5 years post OLT, and the change of AUC through time was graphically depicted for all the scores in terms of graft loss and mortality. The Youden's J statistic was applied to the ROC curves that provided the best results, in order for the optimal cut-off point to be identified. Based on the optimal cut-off points, patients were divided into groups. Kaplan-Meier curves and the log-rank test were used for the assessment and comparison of graft and patient survival between patient groups. Cox regression was used for multivariable graft and patient survival analysis. All the tests were two-tailed. The level of statistical significance was set at alpha=0.05. Because the number of missing values was very low [97 out of 18209 values (0.53%) and the percentage of patients with at least one missing value was also low [62 out of 1017 patients (6.1%)], we excluded cases pairwise for univariate analyses and listwise for multivariate analyses. The version 4.0.0 of the R Statistical Software (R Foundation for Statistical Computing, Vienna, Austria) was used for the time-dependent ROC analysis and the 25th edition of the Statistical Package for Social Sciences (SPSS) (IBM Corporation, Armonk, NY, USA) was used for the rest of the statistical analysis.

RESULTS

Time-dependent ROC analysis concerning graft survival

Time-dependent ROC analysis did not provide statistically significant results in regards to graft survival at 1, 3 or 5 years post OLT for any of the tested scores, as

95% CI included values on both sides of 0.5. Furthermore, 95% CI contained values on both sides of 0.5 for the whole length of the AUC graphs (Figure 1). In addition, the combination of donor age or of the sum of donor and recipient age with MELD or UKELD score did not improve their predictive ability concerning graft survival. No significant differences were detected when we compared MELD with UKELD score, D-MELD with D-UKELD score or DR-MELD with DR-UKELD score. The exact results of time-dependent ROC analysis in terms of graft survival are shown in Table 2.

Time-dependent ROC analysis regarding patient survival

Time-dependent ROC analysis did not provide statistically significant results in regards to patient survival at 1, 3 or 5 years post OLT for either MELD or UKELD score, as 95% CI included values on both sides of 0.5. This was also true for the whole length of their AUC graphs (Figure 2). However, outcomes were different when donor age or the sum of donor and recipient age were added to MELD and UKELD scores. In particular, D-MELD and D-UKELD scores resulted in a statistically significant, although low, AUC at 1 year post OLT (D-MELD: AUC: 0.588, 95% CI: 0.52-0.657, D-UKELD: AUC: 0.58, 95% CI: 0.517-0.643). As it can be seen in their AUC graphs, they lost statistical significance after the second postoperative year (Figure 2). As far as DR-MELD and DR-UKELD scores are concerned, they provided higher AUCs in comparison with the rest scores, although still low. Their highest AUC values corresponded to the first postoperative year [DR-MELD: AUC: 0.598, 95% CI: 0.529-0.667, DR-UKELD: AUC: 0.609, 95% CI: 0.549-0.67], as it can be seen in their AUC graphs (Figure 2). Figure 3 depicts ROC

curves for DR-MELD and DR-UKELD scores regarding death within the first year post OLT.

The addition of donor age to either MELD or UKELD score did not significantly increase the predictive ability concerning patient survival. The addition of the sum of donor and recipient age to either MELD or UKELD score increased the predictive ability significantly regarding patient survival at 1 ($p<0.001$) and 3 years ($p=0.038$) post OLT for DR-MELD score and at 1 ($p=0.046$), 3 ($p=0.037$) and 5 years ($p=0.031$) for DR-UKELD score. Nevertheless, no significant differences were detected when we compared MELD with UKELD score, D-MELD with D-UKELD score or DR-MELD with DR-UKELD score. The exact results of time-dependent ROC analysis in terms of patient survival are shown in Table 3.

Patient survival analysis based on DR-MELD score

The mean surveillance period was 1558.9 days (SD: 1227.9) and the median surveillance period was 1323 days (min-max: 0-4318) for the entire cohort. After the application of the Youden's J statistic to the ROC curve for DR-MELD score at 1 year post OLT, a DR-MELD score of 2345 was chosen as the optimal cut-off point. 847 (83.3%) patients had DR-MELD≤2345 and 170 (16.7%) patients had DR-MELD>2345. When follow-up was truncated at 1 year post OLT, recipients with DR-MELD>2345 had shorter patient survival (mean: 314.9 days, SE: 8.8, 95% CI: 297.6-332.2, median: not reached yet) than recipients with DR-MELD≤2345 (mean: 347.4 days, SE: 2.5, 95% CI: 342.6-352.2, median: not reached yet) ($p<0.001$) by 32.5 days on average (Figure 4a). A DR-MELD>2345 remained an independent prognostic factor of worse patient survival within the first postoperative year in the multivariable Cox regression analysis (HR: 2.263, 95% CI: 1.257-4.074, $p=0.007$) (Table 4).

When the optimal cut-off point for predicting 1-year patient survival was applied to the overall patient survival, recipients with DR-MELD>2345 had still shorter patient survival (mean: 3227.1 days, SE: 152.9, 95% CI: 2927.4-3526.7) than recipients with DR-MELD≤2345 (mean: 3535.6 days, SE: 59.8, 95% CI: 3418.4-3652.7) (p=0.005) by 308.5 days on average. Analysing the Kaplan-Meier curves identified deviation between the curves in the first postoperative year, but they were parallel after the second postoperative year (Figure 4b). Thus, the impact on patient survival during the initial postoperative period caused by the higher DR-MELD score was not enough to produce significant difference in the overall patient survival, as it was also shown in the multivariable Cox regression analysis (HR: 1.523, 95% CI: 0.972-2.387, p=0.067) (Table 5).

Patient survival analysis based on DR-UKELD score

After the application of the Youden's J statistic to the ROC curve for DR-UKELD score at 1 year post OLT, a DR-UKELD score of 5908 was chosen as the optimal cut-off point. 646 (63.5%) patients had DR-UKELD≤5908 and 371 (36.5%) patients had DR-UKELD>5908. When follow-up was truncated at 1 year post OLT, recipients with DR-UKELD>5908 had shorter patient survival (mean: 332.5 days, SE: 4.9, 95% CI: 322.9-342.1, median: not reached yet) than recipients with DR-UKELD≤5908 (mean: 347.3 days, SE: 2.9, 95% CI: 341.7-352.9, median: not reached yet) (p=0.002) by 14.8 days (Figure 5a). Nevertheless, a DR-UKELD>5908 did not remain an independent prognostic factor of worse patient survival within the first postoperative year in the multivariable Cox regression analysis (HR: 1.588, 95% CI: 0.966-2.611, p=0.068) (Table 4).

When the optimal cut-off point for predicting 1-year patient survival was applied to the overall patient survival, recipients with DR-UKELD>5908 had still shorter patient survival (mean: 3274.2 days, SE: 105.2, 95% CI: 3067.9-3480.4) than recipients with DR-UKELD≤5908 (mean: 3583.8 days, SE: 65.4, 95% CI: 3455.6-3711.9) (p=0.007) by 309.6 days on average. Analysing the Kaplan-Meier curves identified deviation between the curves in the first postoperative year, but they were parallel after the second postoperative year (Figure 5b). Thus, the impact on patient survival during the initial postoperative period caused by the higher DR-UKELD score was not enough to produce significant difference in the overall patient survival, as it was also shown in the multivariable Cox regression analysis (HR: 1.339, 95% CI: 0.946-1.894, p=0.1) (Table 5).

DISCUSSION

The aim of our study was to assess the ability of MELD and UKELD scores, as well as scores derived from them, to predict graft loss and mortality post OLT. We also aimed to investigate if the predictive ability of MELD and UKELD scores improves after adding donor age or the sum of donor and recipient age to each model. Following the logic behind D-MELD score,[13] we combined a major factor of liver graft quality, namely the donor age, with the severity of recipient's liver failure, as depicted by UKELD score this time, in order to create D-UKELD score. Extending this logic of combining donor and recipient characteristics even further, we modified D-MELD and D-UKELD scores by adding recipient age also in each model and introduced DR-MELD and DR-UKELD scores. We also tried to identify the optimal cut-off points of the scores providing the best results that lead to significant differences regarding survival post OLT.

Our findings are in accordance to the rest of the studies on MELD, UKELD and D-MELD scores, reporting no or poor predictive ability in terms of graft loss and death.[6-12,14] First of all, we found that none of the six tested scores has any actual ability to predict graft loss after OLT. MELD and UKELD scores did not have any ability to predict death after OLT also. However, D-MELD, D-UKELD, DR-MELD and DR-UKELD scores showed some predictive ability, albeit mediocre, in regards to death, but mainly for the first two years post OLT (three years for DR-UKELD score). The highest AUCs were detected at 1 year post OLT, with DR-MELD and DR-UKELD scores providing higher AUCs than D-MELD and D-UKELD, respectively. Another interesting finding was that the improvement in AUCs by the addition of just donor age to MELD or UKELD models was not statistically significant, which agrees with what a few other studies have already reported.[7,9-11] However, the addition of both donor and recipient age to MELD and UKELD scores resulted in a statistically significant improvement in their AUCs. Moreover, MELD and UKELD did not seem to have different predictive ability and the same was true when we compared the scores deriving from them, namely D-MELD with D-UKELD, and DR-MELD with DR-UKELD. Thus, MELD and UKELD have the same predictive ability, which significantly improves in terms of patient survival when both donor and recipient age are added to each model, but it reaches mediocre levels and it is best for 1-year patient survival post OLT.

The mediocre predictive ability of DR-MELD and DR-UKELD in regards to patient survival can be attributed to the fact that donor age, recipient age, MELD and UKELD scores are not the only parameters that affect recipient survival after OLT. Nevertheless, DR-MELD and DR-UKELD could still provide useful information and cut-off points were identified from ROC curves associated with shorter patient

survival within the first year post OLT (2345 for DR-MELD and 5908 for DR-UKELD). Recipients with DR-MELD>2345 lost 1 month of survival within the first postoperative year and around 10 months of overall survival, which corresponds to about one fifth of the mean surveillance period of our study. Recipients with DR-UKELD>5908 lost only two weeks of survival within the first postoperative year, but they lost around 10 months of overall survival. Nonetheless, Kaplan-Meier curves showed that after an initial deviation between the two curves during the first postoperative year, these were running in parallel practically and close to each other after the second postoperative year. As far as multivariable survival analysis is concerned, only DR-MELD score provided statistically significant results and only for the first postoperative year. In particular, DR-MELD>2345 was an independent risk factor of worse patient survival within the first postoperative year, leading to a more than double risk of dying by the end of the first year after OLT (HR: 2.263), but this was not enough to sustain a long-term hit in overall survival. DR-UKELD>5908 was not an independent risk factor of worse 1-year or overall survival.

At this point we would like to mention that there are some clear limitations to this study. Although we included a large cohort of more than 1000 consecutive deceased-donor OLTs and retrieved the relevant information from our prospectively maintained database of transplanted patients, this is a retrospective study based on single site data. An external validation of the newly described scores is also needed using an independent cohort or a national data set. The next step would be to combine MELD and UKELD scores with other already reported risk scores combining additional donor and/or recipient parameters, such as donor risk index,[15] donor quality index,[16] UK donor liver index,[17] UCLA score for DCD liver transplants,[18] UK DCD risk score,[19] etc, and test it on multicentre or national data.

In conclusion, DR-MELD and DR-UKELD scores provide the best, albeit mediocre, predictive ability among the six tested models, especially at 1 year post OLT, but only regarding patient survival and not graft survival. Due to the mediocre predictive ability, none of the tested models can be used on its own for predicting death after OLT. However, a high DR-MELD score can be considered in clinical practice an additional independent risk factor for worse recipient survival within the first postoperative year, but not concerning overall survival. DR-UKELD score does not seem to have a similar use regarding short-term or overall survival. Since this is the first study introducing D-UKELD, DR-MELD and DR-UKELD scores and looking into their predictive role in regards to post-OLT survival, more studies are needed in order this to be elucidated.

CONFLICTS OF INTEREST

There are no conflicts of interest regarding this study.

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Table 1. Patient and transplant characteristics	
Parameter	**Number**
Donor gender	
Male	547 (53.9%)
Female	467 (46.1%)
Donor age (years)	
Mean (SD)	48.1 (16.7)
Median (min-max)	50 (12-85)
Recipient gender	
Male	701 (68.9%)
Female	316 (31.1%)
Recipient age (years)	
Mean (SD)	51.4 (11.6)
Median (min-max)	54 (16-73)
MELD	
Mean (SD)	16.9 (8.7)
Median (min-max)	15 (6-74)
UKELD	
Mean (SD)	54.6 (7.4)
Median (min-max)	54 (7-80)
D-MELD	
Mean (SD)	814 (542.5)
Median (min-max)	684 (72-5032)
D-UKELD	
Mean (SD)	2623 (983.5)

Median (min-max)	2704 (156-5525)
DR-MELD	
Mean (SD)	1659.2 (916.3)
Median (min-max)	1476 (270-9990)
DR-UKELD	
Mean (SD)	5414.1 (1326.4)
Median (min-max)	5459 (696-9591)
Recipient ethnicity	
White	761 (75.6%)
Asian	144 (14.3%)
Chinese/Oriental	14 (1.4%)
Black	66 (6.6%)
Mixed/Other	22 (2.2%)
Recipient BMI group	
<18.5	27 (2.7%)
18.5-24.9	413 (41.3%)
25-29.9	345 (34.5%)
30-34.9	156 (15.6%)
≥35	58 (5.8%)
Previous OLT	
No	960 (94.4%)
Yes	57 (5.6%)
Underlying liver disease	
ALD cirrhosis	189 (18.8%)
Acute liver failure	94 (9.3%)

Autoimmune hepatitis	30 (3%)
Primary biliary cirrhosis	49 (4.9%)
Primary sclerosing cholangitis	118 (11.7%)
Chronic hepatitis B	38 (3.8%)
Chronic hepatitis C	89 (8.8%)
HCC (without chronic hepatitis)	86 (8.5%)
HCC and chronic hepatitis B	25 (2.5%)
HCC and chronic hepatitis C	117 (11.6%)
NASH	49 (4.9%)
Cryptogenic cirrhosis	21 (2.1%)
Other	102 (10.1%)
Urgency for OLT	
Elective	882 (87.6%)
Urgent	125 (12.4%)
Donor type	
DBD	849 (83.5%)
DCD	168 (16.5%)
Liver steatosis grade	
No	618 (62%)
Mild	275 (27.6%)
Moderate	103 (10.3%)
Graft type	
Whole liver	945 (94%)
Split liver	60 (6%)
OLT technique	

Caval replacement Piggyback	432 (42.9%) 574 (57.1%)
CIT (hours) Mean (SD) Median (min-max)	 8.8 (3.4) 8.1 (1.5-26.7)
Graft losses	129 (12.7%)
1-year graft survival rate	91%
3-year graft survival rate	89%
5-year graft survival rate	86%
Deaths	175 (17.2%)
1-year patient survival rate	91%
3-year patient survival rate	87%
5-year patient survival rate	83%

MELD: Model for end-stage liver disease, UKELD: United Kingdom model for end-stage liver disease, BMI: body mass index, OLT: orthotopic liver transplant, ALD: alcoholic liver disease, HCC: hepatocellular carcinoma, NASH: non-alcoholic steatohepatitis, DBD: donation after brain death, DCD: donation after circulatory death, CIT: cold ischaemia time

Table 2. Time-dependent ROC analysis concerning graft survival

Score	**AUC (95% CI)**		
	1 year	**3 years**	**5 years**
MELD	0.536 (0.472-0.6)	0.526 (0.464-0.587)	0.516 (0.453-0.579)
D-MELD	0.526 (0.462-0.591)	0.532 (0.47-0.593)	0.535 (0.471-0.598)
DR-MELD	0.539 (0.475-0.603)	0.534 (0.473-0.596)	0.529 (0.466-0.593)
UKELD	0.53 (0.466-0.595)	0.505 (0.444-0.565)	0.478 (0.417-0.54)
D-UKELD	0.518 (0.453-0.582)	0.522 (0.459-0.586)	0.526 (0.464-0.588)
DR-UKELD	0.54 (0.476-0.605)	0.536 (0.472-0.601)	0.519 (0.457-0.58)
Comparison	**P-value**		
	1 year	**3 years**	**5 years**
MELD vs D-MELD	0.69	0.789	0.363
MELD vs DR-MELD	0.849	0.575	0.36
UKELD vs D-UKELD	0.747	0.634	0.182
UKELD vs DR-UKELD	0.788	0.374	0.244
MELD vs UKELD	0.759	0.3	0.06
D-MELD vs D-UKELD	0.687	0.686	0.688
DR-MELD vs	0.948	0.946	0.7

DR-UKELD			

ROC: receiver operating characteristic, AUC: area under curve, CI: confidence intervals, MELD: Model for end-stage liver disease, UKELD: United Kingdom model for end-stage liver disease

Table 3. Time-dependent ROC analysis regarding patient survival

Score	**AUC (95% CI)**		
	1 year	**3 years**	**5 years**
MELD	0.557 (0.486-0.628)	0.528 (0.468-0.588)	0.507 (0.447-0.566)
D-MELD	**0.588 (0.52-0.657)**	0.546 (0.485-0.606)	0.535 (0.475-0.594)
DR-MELD	**0.598 (0.529-0.667)**	0.557 (0.496-0.618)	0.532 (0.472-0.591)
UKELD	0.545 (0.478-0.613)	0.501 (0.442-0.559)	0.473 (0.416-0.53)
D-UKELD	**0.58 (0.517-0.643)**	0.538 (0.479-0.598)	0.535 (0.478-0.592)
DR-UKELD	**0.609 (0.549-0.67)**	**0.567 (0.508-0.627)**	0.543 (0.486-0.599)
Comparison	**P-value**		
	1 year	**3 years**	**5 years**
MELD vs D-MELD	0.094	0.378	0.136
MELD vs DR-MELD	**<0.001**	**0.038**	0.07
UKELD vs D-UKELD	0.344	0.275	0.063
UKELD vs DR-UKELD	**0.046**	**0.037**	**0.031**
MELD vs UKELD	0.494	0.133	0.06
D-MELD vs D-UKELD	0.708	0.727	0.966
DR-MELD vs	0.687	0.676	0.676

DR-UKELD			

ROC: receiver operating characteristic, AUC: area under curve, CI: confidence intervals, MELD: Model for end-stage liver disease, UKELD: United Kingdom model for end-stage liver disease

Table 4. Multivariable Cox regression analysis of factors associated with 1-year patient survival

Parameter	**DR-MELD**			**DR-UKELD**		
	HR	**95% CI**	**P-value**	**HR**	**95% CI**	**P-value**
DR-MELD [reference: DR-MELD≤2345]						
DR-MELD>2345	2.263	1.257-4.074	**0.007**			
DR-UKELD [reference: DR-UKELD≤5908]						
DR-UKELD>5908				1.588	0.966-2.611	0.068
Recipient gender (reference: female)						
Male	0.783	0.469-1.308	0.35	0.796	0.476-1.33	0.383
Recipient ethnicity (reference: White)						
Asian	1.556	0.822-2.945	0.175	1.533	0.807-2.91	0.192
Chinese/Oriental	2.417	0.537-10.865	0.25	2.066	0.466-9.168	0.34
Black	2.202	1-4.846	0.05	2.205	0.997-4.877	0.051
Mixed/Other	1.728	0.49-6.096	0.395	2.067	0.591-7.23	0.255
Recipient BMI group (reference: 18.5-24.9)						
<18.5	0.349	0.047-2.571	0.301	0.314	0.043-2.316	0.256

25-29.9	0.607	0.34-1.082	0.091	0.594	0.335-1.054	0.075
30-34.9	0.62	0.301-1.277	0.195	0.606	0.296-1.243	0.172
≥35	1.039	0.415-2.6	0.934	1.039	0.417-2.59	0.935
Previous OLT (reference: no)						
Yes	0.856	0.192-3.822	0.839	0.883	0.205-3.81	0.868
Underlying liver disease (reference: ALD cirrhosis)						
Acute liver failure	0.562	0.103-3.058	0.505	0.744	0.138-4	0.73
Autoimmune hepatitis	0.947	0.143-6.278	0.955	0.943	0.14-6.374	0.952
Primary biliary cirrhosis	0.63	0.131-3.035	0.565	0.608	0.128-2.891	0.532
Primary sclerosing cholangitis	0.646	0.217-1.922	0.433	0.631	0.213-1.868	0.405
Chronic hepatitis B	0.664	0.141-3.129	0.605	0.667	0.142-3.13	0.608
Chronic hepatitis C	0.712	0.223-2.27	0.565	0.66	0.207-2.099	0.481
HCC (without chronic hepatitis)	1.899	0.752-4.794	0.175	1.682	0.669-4.232	0.269
HCC and chronic hepatitis B	0.465	0.055-3.937	0.482	0.497	0.059-4.178	0.52
HCC and chronic hepatitis C	1.387	0.548-3.51	0.49	1.361	0.538-3.442	0.514
NASH	3.224	1.259-8.26	**0.015**	2.699	1.043-6.981	**0.041**

Cryptogenic cirrhosis	1.62	0.342-7.666	0.543	1.577	0.327-7.597	0.57
Other	1.496	0.488-4.579	0.481	1.57	0.516-4.781	0.427
Urgency for OLT (reference: elective)						
Urgent	2.579	0.583-11.411	0.212	2.817	0.648-12.245	0.167
Donor type (reference: DBD)						
DCD	1.278	0.637-2.566	0.49	1.188	0.597-2.365	0.623
Donor gender (reference: female)						
Male	1.188	0.717-1.968	0.504	1.177	0.711-1.95	0.526
Liver steatosis grade (reference: no)						
Mild	0.884	0.497-1.575	0.677	0.812	0.45-1.468	0.492
Moderate	2.085	1.082-4.018	**0.028**	1.944	0.999-3.781	0.05
Graft type (reference: whole liver)						
Split liver	1.061	0.395-2.846	0.907	1.014	0.378-2.722	0.977
OLT technique (reference: caval replacement)						
Piggyback	1.003	0.626-1.606	0.991	1.024	0.638-1.643	0.922
CIT (hours)	1.031	0.96-1.107	0.401	1.024	0.953-1.1	0.524

MELD: Model for end-stage liver disease, UKELD: United Kingdom model for end-stage liver disease, BMI: body mass index, OLT: orthotopic liver transplant, ALD: alcoholic liver disease, HCC: hepatocellular carcinoma, NASH: non-alcoholic steatohepatitis, DBD: donation after brain death, DCD: donation after circulatory death, CIT: cold ischaemia time

Table 5. Multivariable Cox regression analysis of factors associated with overall patient survival

Parameter	DR-MELD			DR-UKELD		
	HR	95% CI	P-value	HR	95% CI	P-value
DR-MELD [reference: DR-MELD≤2345]						
DR-MELD>2345	1.523	0.972-2.387	0.067			
DR-UKELD [reference: DR-UKELD≤5908]						
DR-UKELD>5908				1.339	0.946-1.894	0.1
Recipient gender (reference: female)						
Male	0.846	0.588-1.218	0.369	0.861	0.598-1.239	0.42
Recipient ethnicity (reference: White)						
Asian	1.108	0.701-1.75	0.661	1.099	0.695-1.739	0.686
Chinese/Oriental	1.629	0.368-7.218	0.52	1.5	0.342-6.574	0.591
Black	1.424	0.786-2.579	0.244	1.388	0.765-2.521	0.281
Mixed/Other	2.028	0.844-4.872	0.114	2.275	0.953-5.429	0.064
Recipient BMI group (reference: 18.5-24.9)						
<18.5	0.25	0.061-1.028	0.055	0.244	0.059-1.003	0.051

25-29.9	0.774	0.531-1.129	0.184	0.766	0.526-1.116	0.165
30-34.9	0.612	0.369-1.014	0.057	0.608	0.368-1.007	0.053
≥35	0.809	0.381-1.719	0.582	0.789	0.372-1.677	0.539
Previous OLT (reference: no)						
Yes	0.862	0.315-2.364	0.773	0.894	0.329-2.429	0.826
Underlying liver disease (reference: ALD cirrhosis)						
Acute liver failure	0.692	0.201-2.375	0.558	0.83	0.243-2.836	0.766
Autoimmune hepatitis	0.24	0.032-1.822	0.168	0.245	0.032-1.863	0.174
Primary biliary cirrhosis	0.588	0.196-1.766	0.344	0.591	0.197-1.774	0.349
Primary sclerosing cholangitis	0.875	0.443-1.727	0.7	0.901	0.456-1.783	0.765
Chronic hepatitis B	0.361	0.084-1.556	0.172	0.368	0.085-1.588	0.18
Chronic hepatitis C	1.43	0.771-2.652	0.257	1.417	0.764-2.627	0.269
HCC (without chronic hepatitis)	2.207	1.166-4.178	**0.015**	2.141	1.132-4.051	**0.019**
HCC and chronic hepatitis B	0.558	0.121-2.584	0.456	0.603	0.131-2.778	0.516
HCC and chronic hepatitis C	1.871	1.039-3.368	**0.037**	1.921	1.063-3.472	**0.031**
NASH	2.228	1.043-4.759	**0.039**	2.017	0.941-4.325	0.071

Cryptogenic cirrhosis	2.527	0.996-6.408	0.051	2.572	1.012-6.536	**0.047**
Other	1.698	0.786-3.667	0.178	1.769	0.818-3.829	0.147
Urgency for OLT (reference: elective)						
Urgent	1.917	0.671-5.471	0.224	1.968	0.692-5.591	0.204
Donor type (reference: DBD)						
DCD	1.161	0.728-1.85	0.531	1.127	0.709-1.792	0.613
Donor gender (reference: female)						
Male	1.023	0.73-1.435	0.894	1.031	0.734-1.449	0.859
Liver steatosis grade (reference: no)						
Mild	1.022	0.7-1.49	0.912	0.958	0.652-1.409	0.829
Moderate	1.925	1.212-3.058	**0.006**	1.81	1.131-2.898	**0.013**
Graft type (reference: whole liver)						
Split liver	0.747	0.333-1.678	0.48	0.749	0.333-1.684	0.484
OLT technique (reference: caval replacement)						
Piggyback	0.939	0.682-1.294	0.701	0.939	0.681-1.295	0.702
CIT (hours)	1.002	0.949-1.059	0.931	0.999	0.944-1.056	0.958

MELD: Model for end-stage liver disease, UKELD: United Kingdom model for end-stage liver disease, BMI: body mass index, OLT: orthotopic liver transplant, ALD: alcoholic liver disease, HCC: hepatocellular carcinoma, NASH: non-alcoholic steatohepatitis, DBD: donation after brain death, DCD: donation after circulatory death, CIT: cold ischaemia time

FIGURE LEGENDS

Figure 1a. Graph of AUCs for MELD, D-MELD, DR-MELD scores against time concerning graft survival

Figure 1b. Graph of AUCs for UKELD, D-UKELD, DR-UKELD scores against time concerning graft survival

Figure 2a. Graph of AUCs for MELD, D-MELD, DR-MELD scores against time regarding patient survival

Figure 2b. Graph of AUCs for UKELD, D-UKELD, DR-UKELD scores against time regarding patient survival

Figure 3. ROC curves for DR-MELD and DR-UKELD scores in terms of mortality within the first postoperative year

Figure 4a. Patient survival within the first postoperative year according to DR-MELD score

Figure 4b. Overall patient survival according to DR-MELD score

Figure 5a. Patient survival within the first postoperative year according to DR-UKELD score

Figure 5b. Overall patient survival according to DR-UKELD score

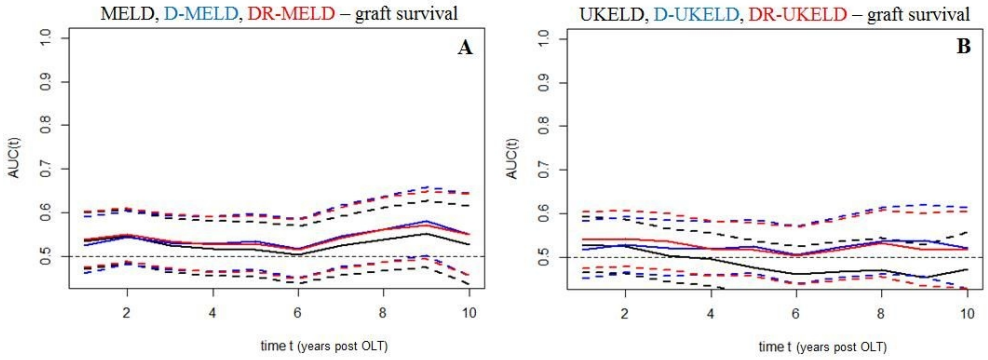

Figure 1a. Graph of AUCs for MELD, D-MELD, DR-MELD scores against time concerning graft survival
Figure 1b. Graph of AUCs for UKELD, D-UKELD, DR-UKELD scores against time concerning graft survival

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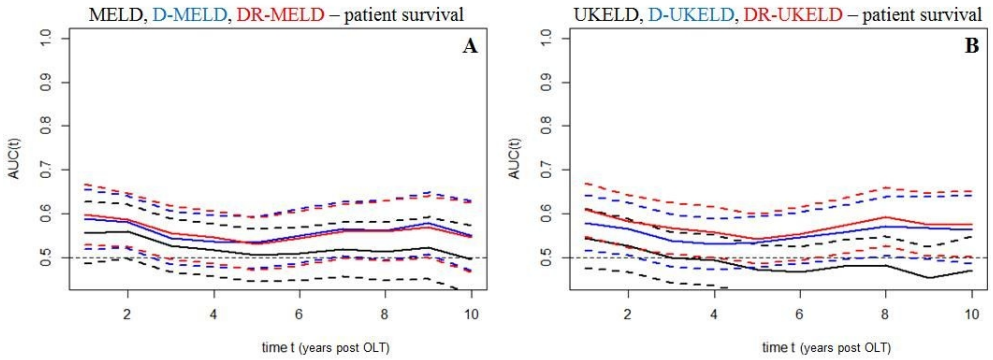

Figure 2a. Graph of AUCs for MELD, D-MELD, DR-MELD scores against time regarding patient survival
Figure 2b. Graph of AUCs for UKELD, D-UKELD, DR-UKELD scores against time regarding patient survival

90x36mm (300 x 300 DPI)

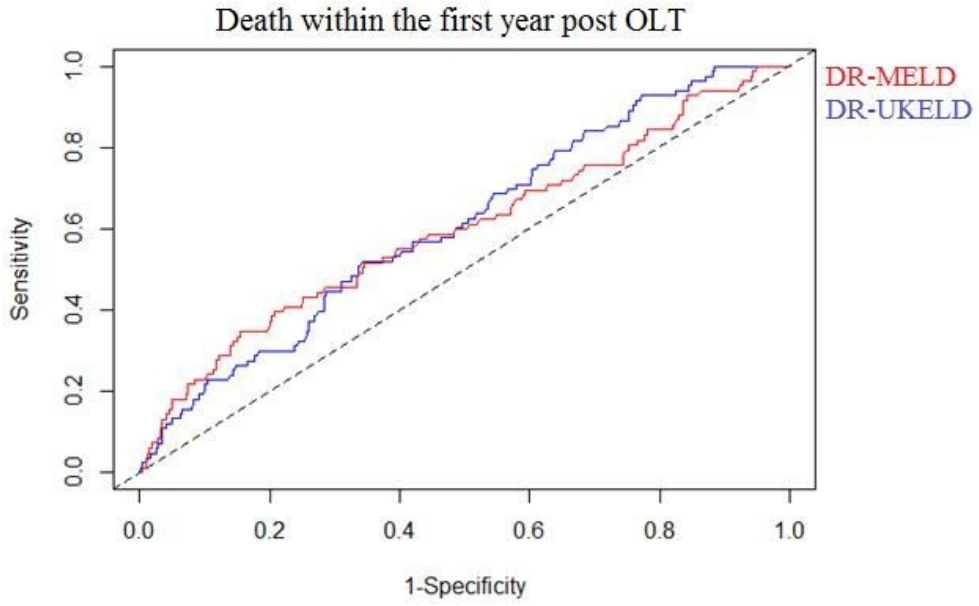

Figure 3. ROC curves for DR-MELD and DR-UKELD scores in terms of mortality within the first postoperative year

53x36mm (300 x 300 DPI)

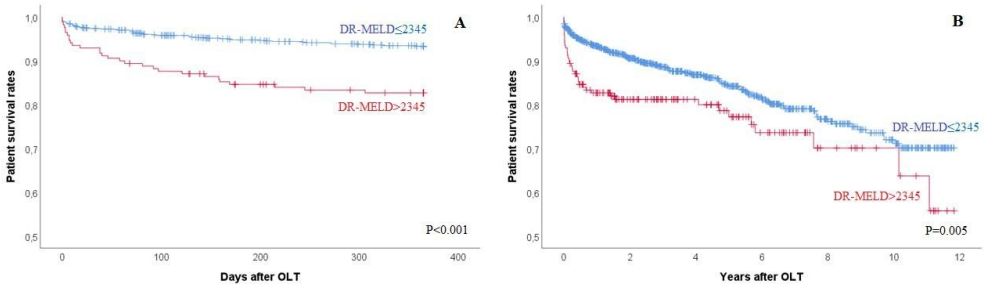

Figure 4a. Patient survival within the first postoperative year according to DR-MELD score
Figure 4b. Overall patient survival according to DR-MELD score

108x31mm (300 x 300 DPI)

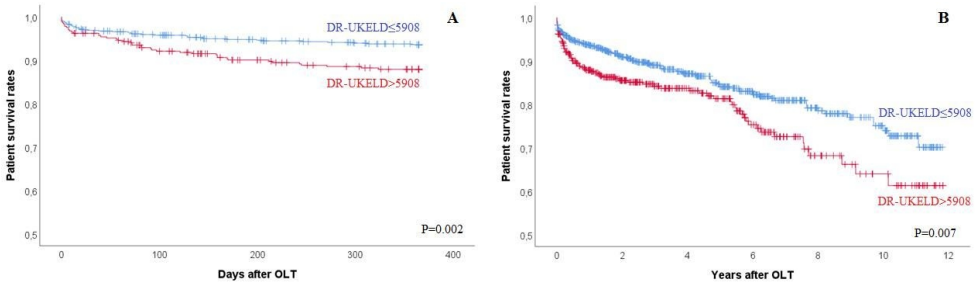

Figure 5a. Patient survival within the first postoperative year according to DR-UKELD score
Figure 5b. Overall patient survival according to DR-UKELD score

109x31mm (300 x 300 DPI)