ELSEVIER

Should a Lower Quality Organ Go to the Least Sick Patient? Model for End-Stage Liver Disease Score and Donor Risk Index as Predictors of Early Allograft Dysfunction

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ABSTRACT

Background. There is a global tendency to justify transplanting extended criteria organs (ECD; Donor Risk Index [DRI] ≥1.7) into recipients with a lower Model for End-Stage Liver Disease (MELD) score and to transplant standard criteria organs (DRI < 1.7) into recipients with a higher MELD scores. There is a lack of evidence in the current literature to justify this assumption.

Methods. A review of our prospectively entered database for donation after brain death (DBD) liver transplantation (n = 310) between January 1, 2006, and September 30, 2010, was performed. DRI was dichotomized as <1.7 and ≥1.7. Recipients were divided into 3 strata, those with high (≥27), moderate (15–26), and low MELD (<15) scores. The recently validated definition of early allograft dysfunction (EAD) was used. We analyzed EAD and its relation with donor DRI and recipient MELD scores.

Results. The overall incidence of EAD was 24.5%. Mortality in the first 6 months in recipients with EAD was 20% compared with 3.4% for those without EAD (relative risk [RR], 5.56, 95% confidence interval [CI], 1.96–15.73; $P < .001$). Graft failure rate in the first 6 months in those with EAD was 27% compared with 5.8% for those without EAD (RR, 4.63; 95% CI, 2.02–10.6; $P < .001$). In patients with low MELD scores, a significantly increased rate of EAD (25%) was seen in patients transplanted with a high DRI liver compared with those transplanted with a low DRI liver (6.25%; $P = .012$). In moderate and high MELD recipients, there was no significant difference in the rate of EAD in patients transplanted with a high DRI liver (62%) compared with those transplanted with a low DRI liver (59%).

Conclusion. These results suggest that contrary to common belief it is not justified to preferentially allocate organs with higher DRI to recipients with lower MELD scores.

TO BRIDGE THE GAP between limited organ supply and the pool of waiting list candidates the use of liver allografts from extended criteria donors (ECD) has continued to grow.[1] Appropriate allocation of these ECD grafts has been widely debated.[2]

With increasing use of ECD organs, it is important to evaluate outcomes to ensure that these organs result in the greatest recipient transplant benefit. The Model for End-Stage Liver Disease (MELD) score was first used in predicting survival in patients after transjugular intrahepatic portosystemic shunt insertions. It has since been shown to be a good predictor of mortality on the liver transplant waiting list and is currently the basis of organ allocation in the United States and several European countries.[3] The Donor Risk Index (DRI) was described in 2006 by Feng et al[4] and was based on donor characteristics associated with an increased risk of graft failure using the SRTR database

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with a large sample size of donors ($n = 20,023$). There is no uniformly accepted definition of what constitutes an ECD allograft; however, previous authors have suggested allografts with a DRI ≥1.7 fulfill this definition.[5]

Traditionally, there has been a trend of transplanting organs with higher DRI in lower MELD patients.[6] This allocation strategy relies on the assumption that increased MELD score amplifies the probability of graft loss inherent to higher DRI allografts. Current literature examining this assumption has shown discrepant results.

An updated definition of early allograft dysfunction (EAD) was recently validated as a predictor of graft and patient survival within 6 months of transplantation. This definition has been shown to be a strong predictor of early graft failure not associated with technical issues or disease recurrence.[7] In the current study we examine the association of recipient MELD score and DRI with EAD.

MATERIALS AND METHODS

After approval from our Institutional Review Board, a review of our prospectively entered database for donation after brain death (DBD) liver transplantation between January 1, 2006, and September 30, 2010, was performed. Candidates initially listed at age <18 and recipients of donation after cardiac death (DCD) and living donor (LD) allografts were excluded.

MELD scores and DRIs were calculated using previously described formulae.[3,4] EAD was defined as the presence of ≥1 of the following postoperative laboratory analyses reflective of liver injury and function: bilirubin, ≥10 mg/dL (171 μmol/L) on day 7, International Normalized Ratio ≥1.6 on day 7, and alanine or aspartate aminotransferases >2000 IU/L within the first 7 days.[7]

DRI was dichotomized as standard liver allografts (DRI <1.7) and ECD liver allografts (DRI ≥1.7). Previous authors have shown that about 25% of liver allografts have a DRI of ≥1.7; therefore, this threshold has been used to define the ECD liver transplant.[5] Recipients were divided into 3 strata based on quartiles, those with high (≥27), moderate (15–26), and low MELD (<15) scores.[5] Patients with hepatocellular carcinoma (HCC) were scored according to synthetic hepatic function and therefore the MELDs used in this study reflect their true MELDs and not adjusted values or exception points. MELD values were at the time of transplant. At present, we do not allocate organs by MELD in Canada. Our allocation system is based on a 4-point scale reflecting severity of illness.[8] Graft failure was defined as recipient death or need for retransplantation or death within 6 months.

Statistical analyses were performed using STATA version 10.0 software (STATA Corp. College Station, Tex). Differences between groups were analyzed using the unpaired t test for continuous variables and by the χ^2 test or continuity correction method for categorical variables. Multivariate-adjusted logistic regression was performed. All statistical tests were considered significant when $P < .05$.

RESULTS

A total of 310 patients underwent deceased donor liver transplant from January 1, 2006, to September 30, 2010. The mean donor age was 45.82 years (SD ±10.07). The average DRI score was 1.50 (SD ± 0.37). Mean recipient age was 54.95 (SD ± 10.07) years. The mean MELD score was 18.98 (SD ± 9.79).

The overall incidence of EAD was 24.5%. Mortality in those with EAD was 20% compared with 3.4% for those without EAD (RR, 5.77; 95% CI, 2.55–13.08; $P < .001$; Table 1). Graft failure rate at 6 months in those with EAD was 27% compared with 5.8% for those without EAD (RR, 4.4; 95% CI, 2.34–8.28; $P < .001$; Table 1). The most common criteria by which recipients met the definition of EAD was elevated bilirubin on POD 7 (73.3%). Sensitivity and specificity for predicting graft failure in those who met the definition of EAD were 59% and 80%, respectively. In addition, sensitivity and specificity for predicting death in those recipients who met the definition of EAD were 65% and 79%, respectively.

In patients with low MELD (<15), a significant increased rate of EAD was seen in patients transplanted with a high DRI liver (≥1.7; 25%) compared with those transplanted with a low DRI liver (<1.7; 6.25%; $P = .012$). In moderate and high MELD recipients, there was no significant difference in the rate of EAD in patients transplanted with a high DRI liver compared with those transplanted with a low DRI liver (Fig 1).

In those recipients who met the criteria for EAD the graft failure rate at 6 months in low, moderate, and high MELD groups was similar, at 24%, 30%, and 26%, respectively. Similarly, the 6-month mortality rate in those meeting the criteria of EAD was also consistent across the 3 groups: Low, 18%; moderate, 24%, and high, 18%. Multivariate logistic regression adjusting for MELD score strata (low, moderate, high) showed that EAD was associated with both the odds of developing graft function at 6 months ($P = .044$) and recipient mortality ($P = .042$).

Multivariate logistic regression, adjusting for recipient age and year of transplant, was performed for the odds of developing EAD. Recipient MELD score was significantly associated with the odds of EAD ($P < .001$) as was the donor DRI ($P = .025$). An interaction term was created between MELD and DRI and this was significantly associated with the odds of EAD ($P < .001$).

DISCUSSION

The number of ECD allografts transplanted in North America continues to grow, reaching close to 24% of the total of donors used in the United States.[9] The most

Table 1. Rate of Graft Failure and Death in Patients Meeting the Definition of EAD Compared with Those Not Meeting the Definition

	EAD ($n = 76$)	No EAD ($n = 234$)	RR	95% CI
Death	15 (20%)	8 (3.4%)	$P < .001$	5.77 (2.55–13.08)
Graft failure	20 (27%)	14 (6.0%)	$P < .001$	4.4 (2.34–8.28)