MELD and living donor liver transplantation outcome

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Abstract

Introduction: MELD score was validated as a predictor of mortality for a wide variety of liver diseases,[8] including cirrhotic patients awaiting liver transplantation (LT).[9] we try to assess the impact of MELD score on patient survival and morbidity post living donor liver transplantation (LDLT) .

Design: Retrospective study.

Methodology: Between February 2007 and December 2011, 80 adults patients, randomly selected with ESLD, had living donor liver transplantation. Nine patients were excluded, the remaining 71 patients were divided into two groups. Group 1 included 38 patients with MELD < 20. Group 2 included 33 patients with MELD > 20. We compared both groups as regard operative data (including operative time and intra-operative blood requirement), early post-operative course (including ICU stay, hospital stay, incidence of infection and other morbidity like renal impairment, cardiovascular, respiratory and neurological complications) and patient survival up to 1 July 2012.

Results: Eleven patients died during this study (15.2%): three out of 38 patients (7.8%) in group 1 and 8 out of 33 patients (24.2%) [P=0.02]. Mean hospital stay was 30±14 and 29±18 days in 1st and 2nd group respectively [P=0.937]. The mean ICU stay in group 1 and 2 was 7±3 and 9± 4 days [P=0.315]. Mean operative time in group 1 and 2 was 11.1±2 and 10.6±1.4 hours [P=0.292]. Mean volume of blood transfusion and cellsaver re-transfusion were 8±4 unit and 1668±202 ml respectively in group 1 in comparison to 10±6 unit and 1910±679 ml respectively in group 2 [P = 0.09 and 0.167]. The incidence of infection was 39.4% and 45.4% in group 1 and 2 respectively [P=0.48]. The incidence of systemic complications (renal, respiratory, cardiovascular and neurological complications) in group 1 and 2 were 36.8 % and 45.5% [P=0.3]

Conclusion: MELD score more than 20 can predict poor overall survival post living donor liver transplantation. No significant relation between MELD score and intra-operative blood requirement, hospital, and ICU stay or post LDLT morbidity was noted.

Introduction:

Orthotopic Liver transplantation (OLT) has become an established treatment approach for patients with end-stage liver diseases (ESLD), but the growing scarcity of grafts compared to numbers of waiting patients, coupled with the high cost of this procedure, make it imperative to make difficult decisions about how to distribute such scarce organs,[1,2] and highlight the need to identify patients likely to have relatively good outcomes after transplantation.[3,4]

The Child-Turcotte-Pugh (CTP) score, originally developed for the assessment of the outcome of patients with cirrhosis and portal hypertension, was extended for general

prognosis, and to stratify patients on the waiting list for LTx.[5]

The use of CTP in prioritizing potential liver transplant recipients is limited by several factors: the variables, ascites and encephalopathy, are all subjective and are influenced by medical therapy. The lack of an assessment of renal function, which is a reliable prognostic marker in cirrhosis, is an additional limiting factor.[6]

The model for end-stage liver disease was initially described by Malinchoc et al.[7] as a mathematical model for predicting survival in the first three months postoperatively for patients who underwent percutaneous placement of transjugular intrahepatic porto-systemic shunt (TIPS). The model for end-stage liver disease (MELD) score was quickly validated as a predictor of mortality for a wide variety of liver diseases,[8] Afterwards, to reduce mortality amongst patients on the waiting list[10] and to eliminate possible confounding factors, the MELD criterion was incorporated as a more transparent and objective system, based on easily measurable laboratory tests.[11]

The ideal allocation system would allocate livers to candidates who are most likely to die without a transplant, but who also have a high probability of survival after OLT.[12] Since February 2002, the United Network for Organ Sharing (UNOS) introduced a new allocation policy for cadaveric liver transplants, based on the model for end stage liver disease (MELD) score.[13] This new policy stratifies the patients based on their risk of death while on the waiting list.[14] The impact of MELD score on postoperative mortality remains elusive.

In this retrospective analysis, we try to assess the impact of MELD score on patient survival and morbidity post living donor liver transplantation (LDLT).

Patients and methods:

Between February 2007 and December 2011, 80 adults patients randomly selected with ESLD (40 patients with MELD less than 20 and 40 patients with MELD more than 20) had living donor liver transplantation at three centers of liver transplantation (Ain Shams center for organ transplant [ASCOT], Wadi Elneel Hospital and Egypt Air hospital) by the same surgical team. Nine patients were excluded, Three had small for size graft, one recipient with combined organ (liver and kidney) transplants and 5 recipients with incomplete follow-up records. The remaining 71 transplants were involved in this study and were followed up by 1 July, 2012.

Seventy patients had living donor liver transplantation with right liver graft (RLG) and one patient had left liver graft. Graft recipient weight ratio (GRWR) was between 0.8 and 1.7. The immunosuppressive regimen included cyclosporine or tacrolimus; mycophenolate mofetil (MMF), and corticosteroids in all patients except those transplanted for HCC the regimen included calcineurin inhibitor and steroid only. Trough levels of cyclosporine were maintained between 250 and 400 ng/ml for the first 1 to 3 months thereafter, 200 to 300 ng/ml. Trough levels of tacrolimus were maintained between 8 and 12 ng/ml. Rapid withdrawal of corticosteroid within three months was routine in all patients (all transplanted for HCV). In cases of acute rejection therapy first consisted of optimization of maintenance level of immunosupression. If not responding MMF or rapamycin might be added if not currently being taken. In some cases shift from cyclosporine to tacrolimus was beneficial. Small dose steroid was used if all other measure failed.

Data analysis:

Seventy one patients included in this study were divided into two groups. Group 1 included 38 patients with MELD score less than 20. Group 2 included 33 patients with MELD score more than 20. MELD score was calculated using laboratory results collected immediately prior to the liver transplantation with no adjustments for malignancy. We calculated the MELD score through the following formula: MELD=(0.957 x ln [creatinine mg/dL]+0.378 x ln [bilirubin mg/dL]+1.12 x ln [INR]+ 0.643 x 108). We examined the age and sex of the recipient,

diagnosis, indication for transplantation, Child-Turcotte-Pugh score, and cold and warm ischemia time. The diagnosis of chronic liver disease was confirmed by histopathology of the explanted liver. The modified Child-Turcotte-Pugh score was calculated and each patient was categorized as A, B, or C. Operative data (including operative time and intra-operative blood transfusion), early post-operative course (including ICU stay, hospital stay, incidence of infection and other morbidity like renal impairment, cardiovascular, respiratory and neurological complications) and patient survival were compared among both groups.

Statistical analysis:

Statistical package for SPSS computer program version 15.0 was used for data analysis. Quantitative variables were summarized using median (range). Qualitative data were summarized using frequencies and percentages. Non-parametric t-test compared means of 2 independent groups. Chi-square and Fisher exact tested proportion independence. Kaplan-Meier method was used to estimate survival and Log rank test to compare curves. p value was significant at <0.05 level.

Results:

This study included 72 patients classified into 2 groups according to MELD score. Demographic data, Child classification, cold and warm ischemia time were comparable between both groups.

MELD score and survival:

Overall patient survival was compared between both groups from date of transplant to the end point of this study in 1 July 2012. Eleven patients died during this study (15.2%): three patients out of 38 (7.8%) in group 1 with MELD less than 20 and 8 patients out of 33 (24.2%) in group 2 with

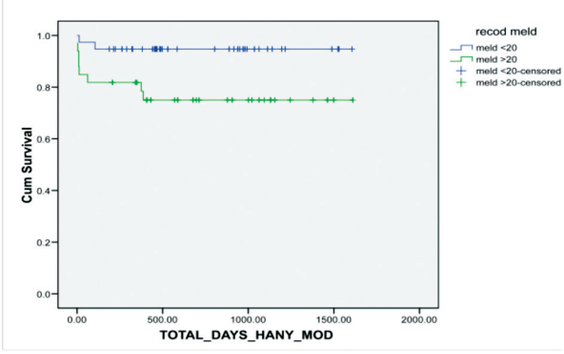

Figure (1): overall survival of both groups.

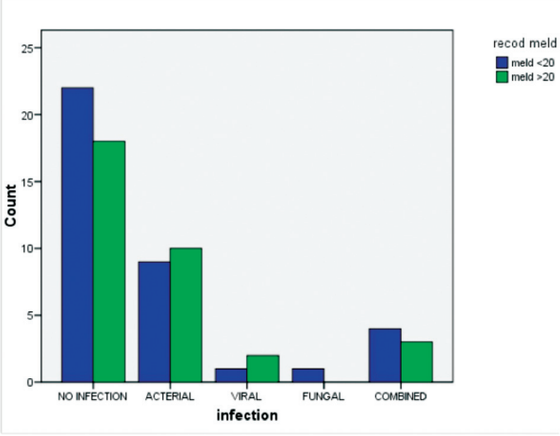

Figure (2): infection rate in both group.

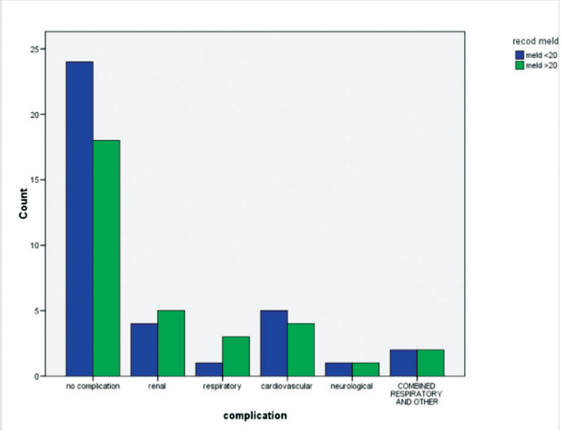

Figure (3)v: incidence of systemic complication in both group.

Table (1): Variables studied.

Variable	MELD < 20	MELD > 20
Age	47.8 ± 7.8	46.2 ± 7.9
Sex		
Male	34 (89.5%)	32 (97%)
Female	4 (10.5%)	1 (3%)
Diagnosis		
ESLD	27 (71.1%)	26 (78.8%)
HCC	3 (7.9%)	0
ESLD + HCC	8 (21%)	7 (21.2%)
Child-turcotte-paugh		
A	0	0
B	3 (7.9%)	0
C	35 (92.1%)	33 (100 %)
Cold ischemia time (min)	47 ± 23	42 ± 30
Warm ischemia time (min)	54.4± 20.2	53.7 ± 16.9

MELD more than 20 [P=0.02]. **Figuer(1)**

MELD score and hospital stay:

In this study a non significant difference was present between both groups as regard hospital stay and ICU stay. In group 1 mean hospital stay was 30±14 days in comparison to 29±18 days in group 2 [P=0.937]. The mean ICU stay in group 1 was 7±3 days while in group 2 mean ICU was 9±4 [P=0.315]

MELD score and operative data:

Comparison between both groups in operative data included operative time, blood loss and intra-operative blood transfusion (cellsaver, blood product) show no statistical significant difference. Mean operative time in group 1 was 11.1±2 hours (ranged between 7–15 hr) and in group 2 was 10.6±1.4 hours (ranged between 9–14 hr) [P=0.292]. mean volume of blood transfusion and cellsaver re-transfusion were 8±4 unit and 1668±202 ml respectively in group 1 in comparison to 10±6 unit and 1910±679 ml respectively in group 2 [P = 0.09 and 0.167].

MELD score and postoperative complication:

Infection:

Overall incidence of infection in this study was 41.6% (30 out of 72 patients). In group 1 with MELD score less than 20 the incidence of infection was 39.4% (15/38 patients). Bacterial infection was the commonest 23.6%, followed by viral 2.6%, fungal 2.6% and combined infection in 10.5%. In group 2 with MELD score more than 20 the incidence of infection was 45.4% (15/33 patients). Bacterial infection was the commonest 30.3%, followed by viral 6%, fungal 0% and combined infection in 9.1%. No statistical significant difference was present between both groups [P=0.48] **Figure(2)**.

Systemic complications:

No significant difference was present between both groups in the incidence of systemic complications including renal, respiratory, cardiovascular and neurological complications (36.8% Vs 45.5%, P=0.3).

Renal impairment was the most common complication in both groups (10.5% in group 1 Vs 15.2% in group 2), followed by cardiovascular complication (13.2% in group 1 Vs 12.1% in group 2) mainly hypertension in most patients and arrhythmia in 2 patients. Neurological complication occurred in 2.6% in group 1 Vs 3% in group 2. Respiratory

complication (basal atelactasis, pleural effusion, adult respiratory distress syndrome and respiratory infection) occurred in 7.9 % in group 1 Vs 15.2% in group 2. Two patients in group 1 (5.3%) and 2 patients in group 2 (6.1%) had combined respiratory and other system complication **Figure(3)**.

Discussion:

The large disparity between patient demand and donated organs is a pressing problem for all transplant surgeons. The best solution to this problem is still in dispute. Unfortunately, prioritizing extremely sick patients make it likely that patients who are not as sick ''will be forced to wait until their condition worsens and their chances for success are also diminished'',[15] and patients who are very sick may have worse post-transplant outcomes than healthier patients.[16] Thus, the optimal system would offer grafts to those who are sufficiently sick to justify the transplantation but not too sick to benefit from it,[17] that is, the urgency of need should be jointly optimized with the likelihood of satisfactory outcomes so as to avoid ''futile transplantation''.[18]

An accurate prognostic model could also help potential transplant recipients and their families make informed decisions by providing them with information on the patient's post-transplant survival probability.[19,20]

MELD was implemented to help prioritize prospective liver allograft recipients. The model's accuracy to predict short-term mortality among patients with end-stage liver disease has been largely established.[21] However, an ideal selection system would incorporate predictions for survival while on the waiting list as well as following transplantation. The development of a model that could predict post-transplantation outcome based on pre-transplant variables is inherently difficult because of variation in surgical skills, chance events that occur in the perioperative period, and other factors, such as graft rejection, biliary and vascular complications, that are generally independent of pre-transplant events. Although it might seem plausible that the limited number of pretransplant variables that constitute MELD could probably influence the immediate post-transplant phase, their ability to predict long term outcome would appear less likely. Recently, several investigators examined the predictive value of MELD for post-transplantation outcome, but the results were conflicting and follow-up was limited to 1-2 years, and thus a clear consensus has not yet emerged.[22,23]

In a systematic review about the performance of MELD in the setting of LT, Colongita et al. concluded that MELD score is not a good predictor for short-term mortality after LT and that further studies were needed to assess long term performance.[9] also Batista et al. demonstrated that the preoperative MELD score showed low overall accuracy for predicting survival after liver transplantation, similar to that described in other Brazilian studies.[24] On the other hand, worse survival in recipients with higher MELD scores has been cited by some authors.[25,26,27] This study confirmed the relation between MELD score and post liver transplantation survival. Incidence of mortality was 7.8% in patients with MELD less than 20 in comparison to 24.2% in patients with MELD more than 20 [P= 0.02].

Our study showed no significant impact of MELD score on hospital and ICU stay, comparable with the result of Poon et al.,[28] while a lot of studies like Foxton et al. demonstrated that transplantation of patients with higher MELD scores resulted in an increased ICU stay, overall hospital stay, and need for renal replacement therapy (RRT).[29] Also Buchananet al. showed that patients in the highest MELD group had longer ICU stays than those in lower MELD groups (P = 0.008).[30]

Lee and Chung, and Massicotte et al. concluded that the MELD score did not predict blood losses and blood product requirement during liver transplantation.[31,32] Other like Feng et al. demonstrated that massive blood transfusion during liver transplantation can be predicted by preoperative MELD score.[33] In our study, no definite relation between MELD score and intra-operative blood loss or

requirement of blood transfusion was noted.

In this study, incidence of infection was comparable between both groups with no significant difference between MELD score less or more than 20. This conclusion is the same finding of Li et al.[34] in which Univariate analysis for risk factors for postoperative bacterial and fungal infection showed no statistical significant difference as regard MELD score.

Twenty eight patients suffered from postoperative complications, 13 of them (36.8%) were in the group of MELD less than 20 and 15 (45.5%) were of the group of MELD more than 20 with P value 0.3. The non significant difference can be explained partially by the increased operative mortality in the higher MELD scores.

Conclusion:

MELD score more than 20 can predict poor overall survival post living donor liver transplantation. No significant relation was noted between MELD score and intra-operative blood loss or blood requirement, hospital, and ICU stay or post LDLT morbidity.

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