

ORIGINAL ARTICLE

The introduction of MELD-based organ allocation impacts 3-month survival after liver transplantation by influencing pretransplant patient characteristics

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Summary

Introduction of the model of end-stage liver disease (MELD) for organ allocation has changed the waiting-list management. Despite reports of unaffected survival after orthotopic liver transplantation (OLT) in the MELD era, survival rates have decreased in our center. The aim of this study was to identify factors contributing to reduced survival. Three-month survival, recipient and graft parameters of all 323 OLT between 2004 and 2008, which fall into a pre- ($N = 220$) and a post-MELD ($n = 103$) era, were analysed by Kaplan–Meier-, Mann–Whitney- and Fisher tests. After the introduction of MELD, mean scores at OLT increased (14.8 vs. 18.6, $P = 0.002$). The main indications for OLT were not statistically different between eras. Post-MELD recipients were older (47.9 vs. 50.9 years, $P = 0.025$), donors younger (NS), cold ischemia time shorter (696 vs. 635 min., $P = 0.001$), and duration of surgery longer (218 vs. 245 min., $P = 0.001$). Procedure time significantly correlated with MELD and international normalized ratio (INR). Three-month survival dropped (from 88.6% to 79.6%, $P = 0.03$). Independent variables of survival were creatinine, urea and duration of surgery. Reduced 3-month survival was associated with longer surgery duration, higher creatinine and urea likely reflecting higher recipient morbidity. Survival probability should be incorporated into MELD-based graft allocation.

Introduction

Against the background of a continued shortage of donor organs, the allocation of liver grafts continues to represent a considerable challenge to transplant hepatology [1]. This challenge is characterized by an attempt to balance the waiting-list mortality aimed at providing a liver transplantation to those with the greatest need on the one hand with that of securing at the same time high probability of a positive outcome and post-transplantation survival of the recipient [2].

In December 2006, Eurotransplant replaced an allocation system based on waiting time and the Child–Turcotte–Pugh (CTP) score by an urgency-based system using the model for end-stage liver disease (MELD) [3]. The anticipated benefit of this change was an improve-

ment of the evaluation of disease severity and a more objective calculation of the underlying score. According to preliminary data from Eurotransplant waiting-list mortality decreased after introduction of the new allocation system. However, transplant centers are now confronted with the challenge of transplant candidates who are suffer from more advanced stages of liver disease.

While MELD predicts mortality on the waiting list before transplantation well [4–6], its prediction of survival after orthotopic liver transplantation (OLT) still remains controversial and some analyses indicate that prediction of post-transplantation mortality is poor [2,7–9]. In the United Kingdom, analyses indicated that delta MELD and hyponatremia were found to predict patients on the waiting list that did not reach transplantation, while MELD was associated with post-transplant outcome

[10]. However, the prediction of post OLT outcome based on pre-OLT parameters is more difficult [11–16]. In most centers, reports indicate that waiting-list mortality has been considerably reduced by implementation of MELD-based allocation criteria [9,17–19]. However, the management of candidates on the waiting list has clearly changed. MELD assigns a high priority to patients with abnormal coagulation, creatinine and serum bilirubin, which generally reflect a high degree of morbidity and selects patients with higher complexity of disease and longer hospital treatment time [20]. In addition, about 15–20% of patients with chronic liver diseases are not predictable in this system [21,22], and patients of more advanced age and with renal failure that would be prioritized for transplantation suffer from a poorer outcome [23]. It has also been reported that renal failure in acute liver failure is more likely to recover after transplantation than in chronic liver failure where renal failure is likely to deteriorate, which is not predicted by pretransplant MELD scores [24]. The probability of survival has also been linked to center volume size [25,26], and an analysis of graft quality and outcome has suggested that patients with the lowest MELD-based priority are likely to receive the organs with higher associated risks [27]. These developments indicate that the prediction of the factors influencing outcome are complex, which has led to the consideration of further development and refinement of the MELD system [17,21,22,28–30].

Following the prioritization of patients with higher lab MELD scores for liver transplantation and an increase of mean MELD scores in our as well as other transplant centers as a result of the implementation of the Eurotransplant criteria in 2006, a decrease of post liver transplantation survival was observed. The aim of this analysis was therefore to investigate recipient and donor associated factors capable of determining outcome after liver transplantation in the MELD-based allocation system, and to thus provide insight into the variables influencing survival.

Materials and methods

Patients

We analysed pretransplant data and 3-month post-transplant survival of all adult (>18 years) OLT recipients at Hannover Medical School between May 1st, 2004, and May 1st, 2008. Living donor transplantations (including domino transplantations), multiple organ transplantations and high urgency transplantations caused by fulminant hepatic failure were excluded. Of the remaining 323 patients 220 were transplanted in the pre-MELD era and 103 patients in the era after the implementation of MELD-based allocation on December 16th, 2006.

There were no differences between both eras regarding surgical technique or the surgical team. Pre- or postoperative patient management (e.g. immunosuppression or preoperative tumor therapy) also did not change during the observation period.

For all patients, data regarding the recipient's age, gender, and etiology of liver disease were collected. Pretransplant biochemical parameters and MELD scores were recorded at the last re-evaluation before OLT, and on the day of OLT. We chose these two time points because parameters obtained at the last re-evaluation were used for organ allocation, while values on the day of transplantation most accurately represent the recipient's overall condition immediately before OLT. Based on the original laboratory data at each time point we calculated a laboratory MELD (labMELD) score as described by Wiesner *et al.* [6]; for patients on dialysis pre-OLT serum creatinine was recorded as 4 mg/dl.

Grafts

To compare the graft quality between the two studied eras of transplant activity we recorded donor age, cold ischemia time, split liver transplantations, gender matching and ABO matching. Additionally, we assessed the total time of duration of transplant surgery as a surrogate parameter for the technical complexity of the procedure.

Outcome

All patients were individually followed for the first 90 days after liver transplantation. Patient death was the primary endpoint of this study; re-transplantation and graft survival were secondary endpoints.

Statistical analysis

Characteristics of patients and grafts in each group were compared with chi-squared test or Fisher's exact test for categorical variables, and with the Mann–Whitney *U*-test for continuous variables. Patient and graft survival was determined by Kaplan–Meier survival analysis and the two groups were compared by log-rank test.

All patient- and graft characteristics that differed statistically significantly between the MELD- and the pre-MELD era were further tested for their influence on outcome: Parameters that individually differed in each group between surviving and deceased patients in the Mann–Whitney *U*-test were entered into a Cox-regression survival analysis. All tests were two-tailed and a *P*-value of 0.05 or less was considered statistically significant. Statistical analyses were performed using the spss 13.0 for Windows (SPSS Inc., Chicago, IL, USA) software.

Results

Recipient characteristics:

The recipient characteristics of the pre-MELD- and the MELD-era are shown in Table 1. Main indications for OLT in both eras were viral hepatitis, alcoholic cirrhosis, primary sclerosing cholangitis (PSC), and hepatocellular carcinoma (HCC). Although there were considerably fewer patients transplanted because of PSC and the number of HCC patients increased, these differences were not statistically significant as determined by Fisher's exact test.

As expected the mean calculated MELD score increased statistically significantly by about 30% in the MELD era.

The MELD scores reported to Eurotransplant and used for organ allocation in the MELD era did not differ significantly from the calculated MELD scores at the time of re-evaluation (mean calculated MELD: 18.9, mean reported MELD: 18.7, $P > 0.05$) and both scores showed a high correlation ($r = 0.996$, $P > 0.001$, Pearson correlation). Of note, 41 patients (39.8%) in the MELD era group, who had received an exceptional MELD (Eurotransplant's standard exception rules), had a mean calculated MELD of only 11.9 ± 4.8 at re-evaluation and of 12.2 ± 4.9 on the day of transplantation, while those 62 patients who received a graft based only upon their reported labMELD status had a mean calculated MELD

Table 1. Recipient variables in the pre-MELD- and the MELD-era.

	pre-MELD era (05/01/2004–12/16/2006), <i>n</i> = 220 % (<i>n</i>)	MELD era (12/17/2006–05/01/2008), <i>n</i> = 103 % (<i>n</i>)	<i>P</i> -value
Diagnosis			
Alcoholic cirrhosis	19.1 (42)	16.5 (17)	0.64
Primary sclerosing cholangitis	19.1 (42)	10.7 (11)	0.07
Hepatitis C	15.9 (35)	15.5 (16)	1
Hepatitis B	10.5 (23)	9.7 (10)	1
Hepatocellular carcinoma*	16.4 (36)	23.3 (24)	0.17
Cryptogenic cirrhosis	6.8 (15)	12.6 (13)	0.09
Primary biliary cirrhosis	6.4 (14)	3.9 (4)	0.44
Hemochromatosis	3.6 (8)	0.97 (1)	0.28
AIH	3.2 (7)	3.9 (4)	0.74
Second. scleros. cholangitis	1.8 (4)	2.9 (3)	0.68
Liver cysts	1.8 (4)	5.8 (6)	0.08
Others†	11.8 (26)	17.5 (18)	0.17
Previous liver transplantation	7.3 (16)	11.7 (12)	0.21
Demographics			
Age [years, mean \pm SD, (median, range)]	47.9 \pm 11.4 [49.4, 20.2–68.8]	50.9 \pm 11.3 [52.1, 18.3–68.8]	0.025
Gender, male (%)	61.8	63.1	0.9
Pretransplant MELD [mean \pm SD, (median, range)]			
At last re-evaluation	14.3 \pm 5.5 [13.4, 6.4–38.3]	18.9 \pm 10 [16.3, 6.4–46.2]	0.001
On day of transplantation	14.8 \pm 6.5 [13.8, 6.4–44.3]	18.6 \pm 9.7 [16.7, 6.4–49.1]	0.002
Biochemistry at last re-evaluation [mean \pm SD, (median, range)]			
Creatinine (μ mol/l)	84.3 \pm 80.7 [72, 36–1161]	112.1 \pm 88 [84, 39–611]	0.0002
Bilirubin (μ mol/l)	70.7 \pm 100.7 [42, 4–907]	165.91 \pm 228 [60, 3–944]	0.026
INR (ratio)	1.39 \pm 0.36 [1.31, 1–3]	1.64 \pm 0.68 [1.39, 1–4]	0.014
Cholinesterase (kU/l)	3.69 \pm 2.12 [3.22, 0.5–10.6]	3.44 \pm 1.99 [2.91, 0.7–10.3]	0.306
Biochemistry on day of transplantation [mean \pm SD, (median, range)]			
Creatinine (μ mol/l)	84.9 \pm 67 [72, 28–911]	103.6 \pm 70 [82, 38–513]	0.002
Bilirubin (μ mol/l)	77.7 \pm 114.2 [42, 5–749]	171 \pm 235.9 [59, 3–850]	0.044
INR (ratio)	1.42 \pm 0.5 [1.3, 0.9–3.7]	1.62 \pm 0.68 [1.43, 0.9–4.5]	0.008
Cholinesterase (ku/l)	3.7 \pm 2.17 [3.1, 0.2–10.5]	3.73 \pm 2.08 [3.2, 0.8–11.4]	0.752
Urea (mmol/l)	6.81 \pm 4.42 [5.5, 2.3–27.4]	10.27 \pm 8.89 [6.9, 2.0–41.4]	0.0008
Sodium (mmol/l)	136.5 \pm 4.9 [137, 118–150]	137.2 \pm 5.1 [138, 123–149]	0.354

The *P*-value was calculated with Fisher's exact test (two-sided) for categorical variables and with Mann-Whitney *U*-test for continuous variables.

*Primary HCC in nine patients. Secondary HCC in patients with Hepatitis C (21), Hepatitis B (14), alcoholic cirrhosis (10), NASH (3) and others (3).

†Others: adenomatosis, chronic cholangitis following Kasai operation because of biliary atresia, glycogenosis, idiosyncratic toxic hepatitis, Budd-Chiari syndrome, Caroli's syndrome, portal vein thrombosis because of prothrombin mutation, focal nodular hyperplasia, porphyria, congenital bile-duct hypoplasia, congenital liver fibrosis, drug-induced liver failure, primary hyperoxaluria, cystic fibrosis, protein-C/S-deficiency. The numbers and *P*-values of significant comparisons are shown in bold.

of 23.5 ± 10 at re-evaluation and one of 22.8 ± 9.8 on the day of transplantation.

The MELD-parameters creatinine, bilirubin and INR were statistically significantly higher in the MELD era both at last re-evaluation and on the day of OLT. Other biochemical parameters associated with a poor liver function such as serum sodium and serum cholinesterase did not change after the implementation of MELD. Urea, a parameter that represents poor kidney function, increased statistically significantly in the MELD era. Furthermore, recipients were statistically significantly older in the MELD era cohort (50.9 vs. 47.9 years), whereas the gender distribution of recipients did not change.

Graft characteristics and surgery

As shown in Table 2 there were no statistically significant changes between the two eras regarding donor age, rate of ABO-compatible but nonmatching grafts (Donor:O/Recipient:B or Recipient:AB/Donor A or B), or the rate of split liver grafts. Transplantations using gender-mismatched organs were performed in about 40% in both eras. The mean cold ischemia time was significantly shorter (635.1 min vs. 696.2 min, $P = 0.001$) in the MELD era. However, mean transplant surgery procedure time increased significantly ($P < 0.00001$) from a mean of 218.4 min in the pre-MELD era to 245 min in the MELD era. This increase in surgery time correlated statistically significantly with a higher INR and a higher MELD on the day of transplantation (Fig. 1).

Post-transplantation patient and graft survival

Patients who were transplanted in the MELD era had a significantly ($P = 0.03$) lower 3-month survival than patients that received the liver graft before the introduction of a MELD-based organ allocation system (79.6% as compared with 88.6% 3-month survival, see Fig. 2a and Table 3).

This difference had an even higher statistical significance (78% vs. 88.7%, $P = 0.016$) when only recipients of a first liver allograft were analysed (Fig. 2b). When patients with an exceptional MELD were excluded from the analysis (Fig. 2a), the remaining 62 patients, who received a graft only based on their reported labMELD, showed an even lower 3-month survival of only 75.8% ($P = 0.009$).

The 3-month graft survival rate also decreased from 80.5% in the pre-MELD era to 74.8% in the MELD era, which was not statistically significant, and because the rate of re-transplantation (around 11%) did not change between eras, the reduced graft survival in the MELD is predominantly a consequence of the lower patient 3-month-survival.

The reasons for patient deaths were not significantly different between both eras, and in most of the cases more than one reason contributed to mortality. The main reason leading to death was septicemia with subsequent multiorgan failure (52.0% pre- and 66.7% post-MELD). Severe hemorrhage leading to massive transfusions with typical complications subsequently such as pulmonary edema accounted for 24% of the deaths during both eras. Twenty eight percent (pre-MELD) and 28.6% (post-MELD) of the deceased patients, respectively, (vs. 8% of the surviving patients, $P < 0.01$) required an urgent retransplantation because of initial nonfunctioning of the graft. However, graft failure led to death in only 20% (pre-MELD) and 5% (post-MELD) respectively. Other less frequent causes of death after liver transplantation were cardiac (8% pre-MELD, 19% post-MELD) or cerebral (16% pre-MELD, 19% post-MELD) events, portal vein thrombosis or pancreatitis.

Parameters impairing post-OLT outcome after MELD implementation

In order to determine which factors caused the decline of the 3-month patient survival in the MELD era, we further

Table 2. Graft variables in the pre-MELD- and the MELD-era.

	pre-MELD era (05/01/2004–12/16/2006) $n = 220$	MELD era (12/17/2006–05/01/2008) $n = 103$	<i>P</i> -value
Donor age [years, mean \pm SD, (median, range)]	50.13 \pm 15.1 [51, 15–82]	48.1 \pm 15.2 [50, 14–80]	0.33
Cold ischemia time [min, mean \pm SD, (median, range)]	696.2 \pm 143.1 [690, 219–1163]	635.1 \pm 160.4 [630, 260–1098]	0.001
transplant surgery time [min, mean \pm SD, (median, range)]	218.4 \pm 67.5 [205, 118–663]	245 \pm 63.5 [235, 128–429]	0.00006
Gender mismatch	40%	38.8%	0.9
ABO-compatible mismatch	0.9%	3.9%	0.08
Split liver graft	10%	7.8%	0.68

The *P*-value was calculated with Fisher's exact test (two-sided) for categorical variables and with Mann-Whitney *U*-test for continuous variables. Significant comparisons are shown in bold.

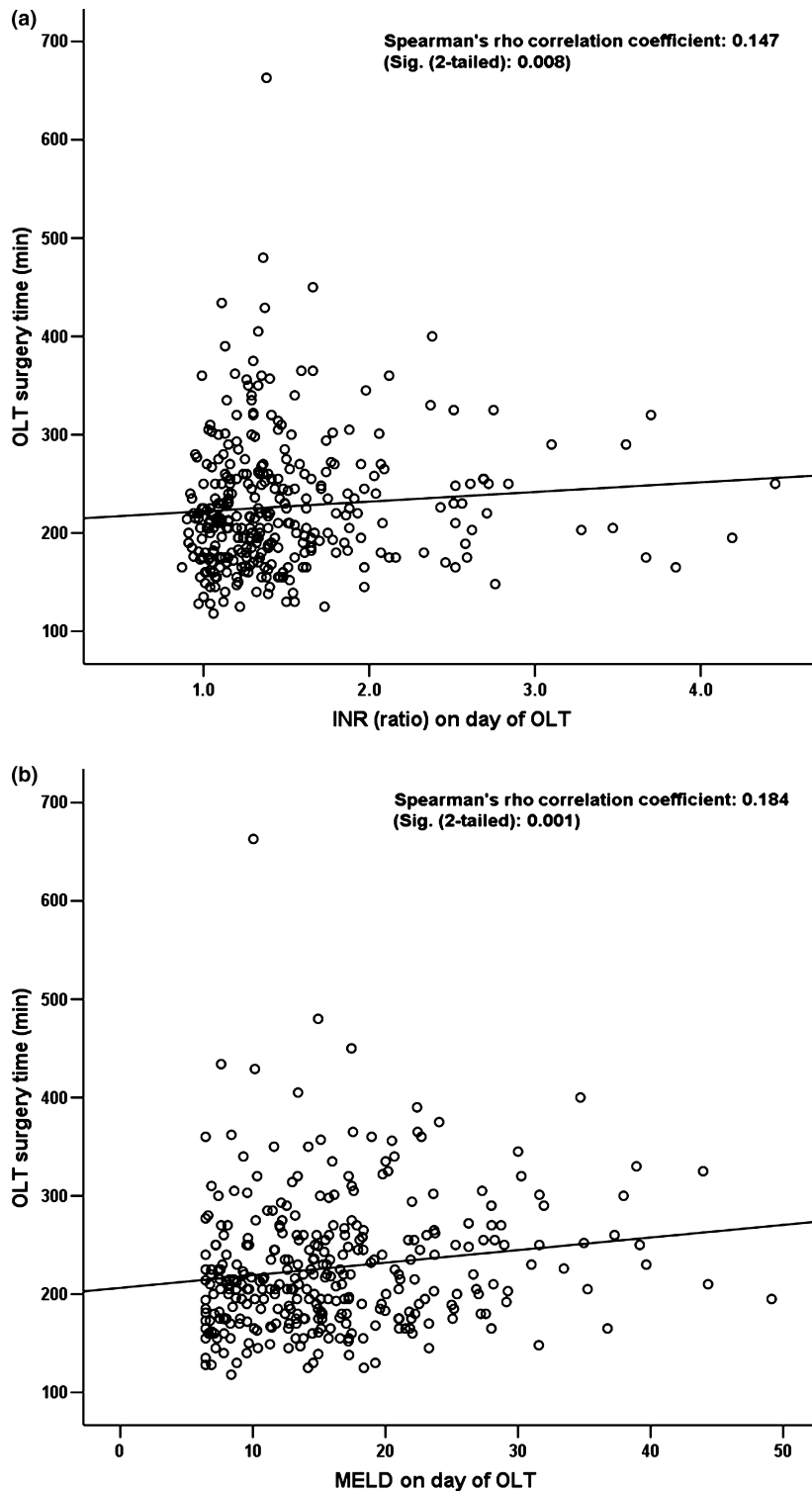


Figure 1 Statistically significant correlation between orthotopic liver transplantation (OLT) surgery time and INR (a) resp. MELD (b) on the day of OLT.

analysed the variables that differed significantly between both eras. At first, by using a univariate test, we identified five factors that differed significantly between patients who died and those who survived in the MELD era as

well as in the pre-MELD era (Table 4a). These factors were included in a backward stepwise Cox regression analysis and finally the parameters OLT surgery time, urea at transplantation and creatinine at re-evaluation

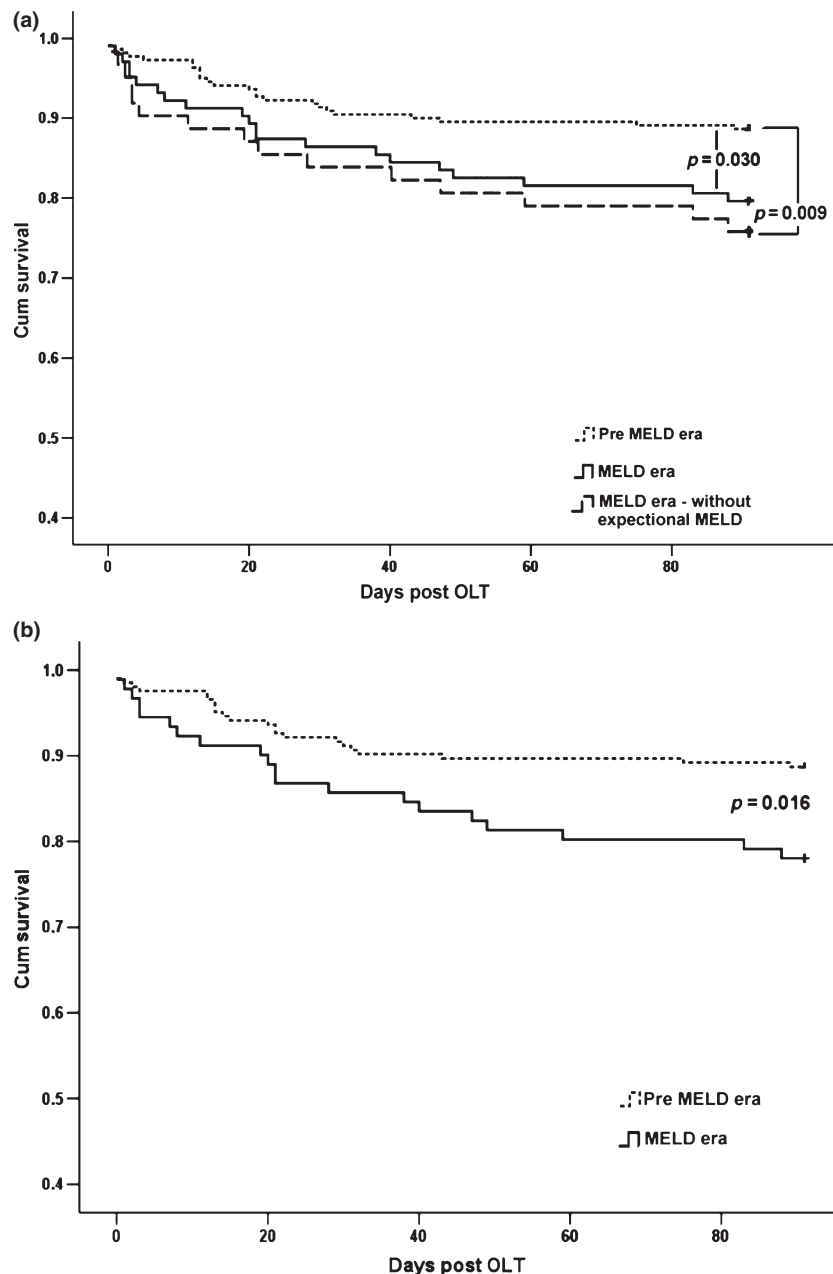


Figure 2 (a) Kaplan–Meier analysis of short-time survival after orthotopic liver transplantation (OLT) for all patients of the pre-MELD-era ($n = 220$) and the MELD-era ($n = 103$) and of the MELD-era after exclusion of patients who received an exceptional MELD ($n = 62$). All patients were followed up for 3 months or until the end point death and therefore numbers at risk are not specified. (b) Kaplan–Meier analysis of short-time survival after OLT only for recipients of a first liver graft of the pre-MELD-era ($n = 204$, 88.7% survival) and the MELD-era ($n = 91$, 78.0% survival). All patients were followed up for 3 months or until the end point death and therefore numbers at risk are not specified.

were identified to be independently correlated with 3-month survival (Table 4b).

Discussion

This is the first in-depth analysis of the impact of the MELD-based organ allocation system on survival after liver transplantation from a single center of the Euro-transplant region and in contrast to a number of other reports [31] from the United States, it reports a statistically significant decrease of short-time survival after liver

transplantation. More precisely the change of allocation criteria from a CTP-based allocation system to the MELD score has resulted in a reduced 3-month-survival in our center, decreasing from 88.6% to 79.6% ($P = 0.031$) for adult recipients of a cadaveric liver transplantation, when data pertaining to a pre-MELD era between 2004 and 2006 was compared with that of a post-MELD era between 2006 and 2008. In this comparison, 90-day graft survival was also reduced, which was not statistically significant, and the rate of re-transplantation was not significantly different. This observation led us to explore in

detail the potential factors that are associated with this development.

Mortality is closely associated with the underlying disease leading to liver transplantation [2]. An increase in

the number of patients with chronic hepatitis C would be expected to lead to higher mortality [2,9,32–34] while an increase of patients with HCC within the Milan criteria [35] would reduce 3-month mortality [36] because of the increased priority associated with granting of a standard exception MELD score. Although the implementation of MELD allocation led to an increase of HCC and cystic liver disease patients and a decrease of patients with primary sclerosing cholangitis the overall disease entities requiring transplantation were not significantly different between both groups excluding this as a relevant factor. When the recipients were analysed, the recipient age was found to be higher in the MELD era, the mean MELD rose from 14.3 to 18.9 and the biochemical profile was significantly different as expected from the definition of MELD. In addition to INR, bilirubin and creatinine, we detected an increase of blood urea nitrogen in the post-MELD group, which is an indicator of more severe renal or nutritional abnormalities. Mortality is also associated with the complexity of the surgery and cold ischemia time, as also with the age of the donor graft [27,33].

Table 3. Outcome variables in the pre-MELD- and the MELD-era.

	pre-MELD era (05/01/2004– 12/16/2006) <i>n</i> = 220	MELD era (12/17/2006– 05/01/2008) <i>n</i> = 103	<i>P</i> -value
Patient survival at day 90 (%)	88.6	79.6	0.030
Graft survival at day 90 (%)	80.5	74.8	0.24
Retransplantation during first 90 days post orthotopic liver transplantation (%)	11.4	10.7	0.86

The *P*-value was calculated with log-rank test for survival analysis and with chi-squared test for retransplantation rate. Bold face indicates a statistically significant comparison.

Table 4. Outcome parameters for 90-day survival.

a)

	pre-MELD era (05/01/2004–12/16/2006) <i>n</i> = 220, mean (median)			MELD era (12/17/2006–05/01/2008) <i>n</i> = 103, mean (median)		
	Survived (<i>n</i> = 195)	Died (<i>n</i> = 25)	<i>P</i>	Survived (<i>n</i> = 82)	Died (<i>n</i> = 21)	<i>P</i>
90 day survival						
Recipients age (years)	47.1 [48.5]	54 [54.3]	0.002	50.9 [52.4]	50.9 [51.5]	0.86
MELD at last re-evaluation	14 [13.2]	16.6 [16.2]	0.092	17.7 [15.7]	23.7 [18.8]	0.058
MELD at transplantation	14.6 [13.4]	16.5 [16.9]	0.059	17.3 [16.2]	23.5 [21.8]	0.037
Cold ischemia time (min)	696.8 [693]	690.8 [676]	0.822	631.5 [634]	650 [606]	0.771
Orthotopic liver transplantation surgery time (min)	214.3 [205]	250.4 [235]	0.015	235.9 [223]	280.3 [270]	0.014
At last re-evaluation						
Creatinine (μmol/l)	76.9 [70]	142.2 [83]	0.031	99.4 [80]	161.6 [102]	0.031
Bilirubin (μmol/l)	68.6 [42]	87.2 [33]	0.658	138.6 [51]	272.1 [87]	0.156
INR (ratio)	1.37 [1.29]	1.53 [1.44]	0.041	1.59 [1.33]	1.83 [1.75]	0.048
On day of transplantation						
Creatinine (μmol/l)	80.1 [69]	122 [85]	0.018	95.1 [78]	136.6 [114]	0.041
Bilirubin (μmol/l)	77.3 [39]	80.8 [53]	0.356	144.6 [50]	274.3 [90]	0.111
INR (ratio)	1.41 [1.29]	1.54 [1.34]	0.277	1.56 [1.37]	1.85 [1.55]	0.043
Urea (mmol/l)	6.6 [5.4]	8.4 [6.7]	0.032	8.6 [6.1]	16.6 [9.3]	0.007

b)

	B	SE	Wald	Sig.	Exp(B)
Orthotopic liver transplantation surgery time (min)	0.007	0.001	20.154	0.000	1.007
Urea at transplantation	0.055	0.017	10.992	0.001	1.057
Creatinine at re-evaluation	0.002	0.001	4.988	0.026	1.002

a) Recipient and graft variables that differed significantly between the pre-MELD- and the MELD-era (see Tables 1 and 2) were analysed regarding 90-day survival. Patients who died within 90 days after OLT were compared with those surviving 90 days by Mann–Whitney *U*-test.

b) Results of a backward stepwise Cox regression analysis including the parameters that were predictive for 90-day survival in both the pre-MELD- and the MELD-era. Surgery time, urea at OLT and creatinine at re-evaluation were found to be independently predictive for 90-day survival. Statistically significant comparisons are given in bold.

While the mean donor graft age did not differ between the groups, cold ischemia time was statistically significantly reduced in the MELD era but mean surgical procedure time was significantly longer. When this was further analysed, we found a significant correlation of mean operation time with INR, and, because INR is a component of MELD, also with MELD. This finding corroborates observations of a higher requirement of transfusions in patients with higher MELD [20] and it is likely that the need for hemostasis prolonged the surgical procedures. It is important to note, that although the disease spectrum did not differ between the compared groups, and cold ischemia time was shorter [9,32] in the MELD group, mortality was nevertheless higher, which was likely to be the result of the more complex morbidity of the recipient. One factor was the aforementioned mean duration of surgery that amounted to a mean of 280.3 min in those patients who died, and to 235.9 min in those who survived, and was thus statistically significantly longer than that recorded for liver transplantations in patients who survived (214.3 min) and who died (250.4 min) within 90 days prior to the MELD era. To expand on the factors that discriminated those patients who died from those who survived, backward stepwise Cox regression analysis was performed on parameters that were associated with 90-day mortality in both groups. In this analysis duration of surgery, blood urea nitrogen and creatinine were found to be independent predictive parameters of 90-day survival after liver transplantation.

Our data demonstrate several aspects that are important for the management of liver transplantation after the change of organ allocation systems to MELD. Patients with a high labMELD have the highest probability of receiving a graft but this study confirms that they also exhibit the highest complexity and severity of disease. MELD encompasses two parameters that in this analysis have been found to be associated not only with the validated prediction of mortality before transplantation [6,37] but appear to also be predictive of 90-day survival: creatinine and INR. It is well known that advanced renal disease increases post-transplantation mortality but it nevertheless is one of the factors that leads to an increase of waiting-list priority. In a recent study, creatinine was also identified as an independent marker of post-transplantation survival together with cholinesterase and age [2]. In addition, elevated urea was found to represent a predictive variable independent of creatinine. Urea not only indicates renal impairment but is also elevated in malnutrition and catabolic metabolism. In our analysis, INR was associated with the length of operation time and this was found to be the third independent variable predicting 90-day mortality. Despite shorter cold ischemia time in the MELD group survival was decreased, which is

likely to be a result of the more complicated surgery in a situation of impaired coagulation. Against this background, it is interesting that a recent study has suggested altering the relative contribution of the two parameters identified in this analysis, INR and creatinine, for the calculation of MELD [28]. In combination, the decrease of 90-day survival in our liver transplantation program following the implementation of MELD-based allocation is associated with an increase of mean MELD scores and has led to an increase of the duration of surgery. The recent suggestion to modify the MELD score regarding INR and creatinine is confirmed in the presented analysis and indicates that the currently employed MELD score based prioritization requires modifications to account for patients with complex morbidity and to optimize post-transplantation survival.

Authorship

TJW: data collection, analysis, writing of paper. AN: data collection, analysis of data. TB: data collection, analysis of data. HBH: data collection, analysis of data. JK: analysis of data. MPM: analysis of data. CPS: analysis of data, writing of paper.

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