

MELD may not be the better system for organ allocation in liver transplantation patients in Singapore

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ABSTRACT

Introduction: The Model for End-Stage Liver Disease (MELD) score is a good predictor of mortality on the liver transplant waiting list and is the current system of organ allocation in the USA. However, a higher MELD may be associated with poorer outcome post-liver transplantation. The aim of this study was to determine if MELD should be implemented as the system for organ allocation for liver transplantation in Singapore.

Methods: There were 46 adult patients who underwent primary liver transplantation at the National University Hospital, Singapore from January 1996 to December 2002. We applied the MELD score to patients who were transplanted and looked for a correlation with survival post-transplant. Patients were followed-up until the most recent visit or death. Survival analysis was performed using Cox regression and Kaplan-Meier method.

Results: The mean age at transplant was 52.7 (SD 2.34) years. The majority of the patients transplanted had Hepatitis B (43 percent). The median MELD score at transplantation was 17 (7-42) and the median Child's score was 11 (6-15). There was a significant correlation between pre-transplant MELD and survival at six months (p-value is 0.037, 95 percent confidence interval [CI] is 1.004-1.13) but not at one year (p-value is 0.065, 95 percent CI is 0.99-1.12). There were no differences in the pre-transplant MELD (odds-ratio [OR] 1, 95 percent CI 0.9-1) as well as survival for patients with and without Hepatitis B (OR 0.72, 95 percent CI 0.22-2.35).

Conclusion: MELD allows livers to be allocated to the patients with the greatest medical urgency but its influence on post-transplant survival should be further clarified so that post-transplant survival is not compromised.

Keywords: hepatitis B, liver transplantation, MELD score, organ allocation

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INTRODUCTION

In 2002, the Organ Procurement and Transplant Network in the United States of America implemented a new system, the Model for End-Stage Liver Disease (MELD), for the allocation of livers for transplantation according to disease severity⁽¹⁾. The reason for this change was a result of two studies which showed that waiting time does not predict mortality on the waiting list for liver transplant^(2,3). MELD was to be superior to the Child-Turcotte-Pugh (CTP) score in predicting three months mortality among patients with chronic liver disease on the liver transplant waiting list⁽⁴⁾.

Currently, the system of organ allocation in Singapore is based upon the CTP scoring system and waiting time. MELD may be a more suitable replacement as it allows livers to be allocated based on medical urgency, and it is a more discriminatory and objective scoring system than the CTP. At the same time, there must be a balance between fairness in organ allocation without compromising post-transplant survival. The aim of our study was to determine the median MELD at which patients are currently being transplanted. We also wanted to determine if there was a correlation between post-transplant survival and pre-transplant MELD and CTP scores. As hepatitis B is the main indication for transplant in Singapore, we wanted to see if there was any difference in MELD scores between patients transplanted for Hepatitis B compared to those with other aetiologies.

METHODS

We retrospectively studied the records of all adult patients who underwent liver transplantation from January 1996 to December 2002 at the National University Hospital, which is the designated and sole liver transplant centre in Singapore. There were no

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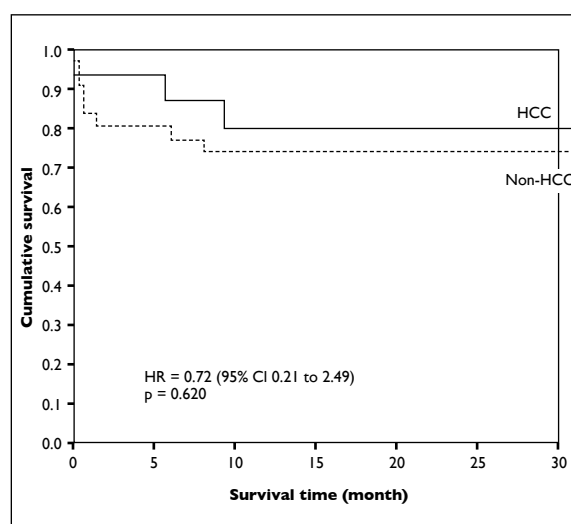
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Table I. Clinical and demographical characteristics of patients.

n=46	
Age in years	
Mean (SD)	52.7 (2.34)
Gender (%)	
Male	37 (80%)
Female	9 (20%)
Race (%)	
Chinese	33 (72%)
Indian	8 (17%)
Malay	1 (2%)
Others	4 (9%)
Type of liver transplant (%)	
Cadaveric	42 (91%)
Living-related, right lobe	2 (4%)
Living-related, left lobe	2 (4%)
Hepatitis B (%)	
Yes	20 (43%)
No	26 (57%)
Hepatocellular carcinoma (%)	
Yes	15 (33)
No	31 (67)
MELD score	
Median (range)	17 (7-42)
Child's score	
Median (range)	11 (6-15)

**Fig. 1** Post-transplant survival of HCC versus non-HCC patients.

re-transplantations. One patient with fulminant hepatic failure and another with pulmonary metastases due to primary hepatocellular carcinoma were excluded from the analysis. Three patients with data unavailable for calculation of pre-transplant MELD

were also excluded. The final study group comprised 46 patients. The MELD immediately pre-transplant were calculated from laboratory results within 24 hours of transplant according to the UNOS formula:

$$\text{MELD} = [0.957 \times \log e (\text{Creatinine}) + 0.378 \times \log e (\text{Bilirubin}) + 1.12 \times \log e (\text{INR}) + 0.643] \times 10.$$

Patients were followed-up until death occurred or until the present time for those who are still alive. We assessed if survival correlated with the pre-transplant MELD scores. We then compared the survival and pre-transplant MELD scores of patients with and without Hepatitis B. Statistical analysis was performed using Cox regression for continuous variables and the Kaplan-Meier method for categorical variables.

RESULTS

The demographical and clinical characteristics of the 46 study patients are shown in Table I. There were altogether 46 adult patients included in this study. The commonest indication for liver transplantation was hepatitis B chronic liver disease with or without hepatocellular carcinoma (HCC). At the time of analysis, 11 deaths were reported. The causes of death include sepsis (36%), primary non-function (36%), ischaemic heart disease with cardiac failure (18%), and hepatic artery thrombosis (9%).

The median MELD score at transplantation was 17 (7-42) and the median Child's score was 11 (6-15). When the survival of patients with and without HCC was compared, we found no difference in survival between the two groups (hazardous ratio [HR] 0.72, 95% CI 0.21-2.49) (Fig. 1). We also found that there was no significant influence of donor age (HR 0.72, 95% CI 0.21-2.49), sex mismatch (HR 0.78, 95% CI 0.23-2.62) and cold ischaemia time (HR 1, 95% CI 0.99-1) on post-transplant survival in our study.

The association between post-transplant survival and pre-transplant MELD score was significant at six months ($p=0.037$, 95% CI 1.004-1.13). The association with post-transplant survival at one year was not significant although there was a trend towards increased mortality with higher pre-transplant MELD scores ($p=0.065$, 95% CI 0.99-1.12). We found no association between the pre-transplant Child's score and post-transplant survival at six months ($p=0.27$, 95% CI 0.88-1.59) or at one year ($p=0.136$, 95% CI 0.93-1.6).

DISCUSSION

In Singapore, the prevalence of hepatitis B is 4% and is the major indication for liver transplantation.

Orthotopic liver transplantation (OLT) has become a viable option since the advent of nucleoside analogues giving excellent outcomes for Hepatitis B patients undergoing OLT. Although the number on the waiting list has grown considerably, this has not been matched by the number of organ donors. Therefore, it is necessary to review our current system of organ allocation such that it is fair and objective, and also allows the best utilisation of resources.

From our single centre study, the median MELD score at transplant was 17, which is similar to the median score of 18 or lower in 92% of liver transplants done in the USA⁽⁵⁾. This appears to be an optimum time for transplantation as the post-transplant survival is good. This gives the physicians an indication when a patient should be worked up for transplant for optimal utilisation of resources. We have also shown that there was no difference in pre-transplant MELD scores and post-transplant survival between patients with hepatitis B and those with other disease aetiologies. This is important as hepatitis B is the main indication for liver transplantation in Singapore and most of Southeast Asia. As MELD is a continuous score, there will be no ambiguity or subjectivity in the allocation of livers. Therefore, there is a strong case for the implementation of MELD in Singapore.

However, our study also shows that post-transplant mortality at six months correlates significantly with pre-transplant MELD. This implies that by transplanting the sickest patients first, we may also be increasing the morbidity and mortality post-liver transplant. A recent study from the USA has shown that post-transplant survival up to two years was significantly lower in groups with higher MELD score⁽⁶⁾. In our study, there was only a trend towards higher mortality at one year with higher MELD scores. This may be because pre-transplant disease severity has the most impact in the early period post-transplant while mortality in the later

period is influenced by other factors such as disease recurrence and chronic rejection. In addition, Saab et al⁽⁷⁾ found that a significant increase rate of death in recipients of OLT with MELD scores higher than 36. However, whether a pre-transplant MELD of 36 should be the cut-off point for liver transplantation, this must be validated in a prospective study. We did not find any significant correlation between the pre-transplant Child's score and post-transplant mortality at six months and one year.

In conclusion, the MELD is more discriminatory, objective and a better predictor of mortality on the liver transplant waiting list than the Child's score. It is indeed a fairer and more transparent system of organ allocation. However, in view of its influence on post-transplant survival, it is necessary to ascertain if there is a MELD score beyond which liver transplantation would be futile.

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