

# Use of the Model for End-Stage Liver Disease (MELD) score to predict 1-year survival of Japanese patients with cirrhosis and to determine who will benefit from living donor liver transplantation

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**Background.** Consideration of the prognosis of patients with liver cirrhosis is important when determining the appropriate timing of liver transplantation. Especially in Japan, where 99% of liver transplants are from living donors, timing is very important not only for the patient but also for the family, who need time to consider the various factors involved in living donations. **Methods.** To clarify the applicability of the Model for End-Stage Liver Disease (MELD) score in Japanese patients with cirrhosis, changes in the MELD score over 24 months were reviewed in 79 patients with cirrhosis who subsequently died of liver failure ( $n = 33$ ) or who survived 24 months ( $n = 46$ ). All patients had Child class B or C cirrhosis at the start of follow-up. We also compared their survival with that of 30 patients treated by living donor liver transplantation (LDLT) in our institute to determine the proper timing of transplantation in patients with cirrhosis. **Results.** Significant stratification of survival curves was observed for MELD scores of <12, 12–15, 15–18, and >18 ( $P = 0.0018$ ). A significant survival benefit of LDLT was observed in patients with MELD score  $\geq 15$  ( $P = 0.0181$ ), and significantly more risk with transplantation was observed in those with MELD score <15 compared with that of patients in whom the disease followed its natural course ( $P = 0.0168$ ). **Conclusions.** MELD score is useful for predicting 1-year survival in Japanese patients with cirrhosis. MELD scores of 15 had discriminatory value for indicating a survival benefit to be gained by liver transplantation and thus can be used to help patients and their families by identifying patients who would benefit from LDLT.

**Key words:** liver cirrhosis, MELD score, living donor liver transplantation, 1 year survival

## Introduction

Liver cirrhosis is an irreversible liver disorder. It causes severe complications such as refractory ascites,<sup>1–3</sup> esophagogastric varices,<sup>4,7</sup> hepatic encephalopathy,<sup>8</sup> and spontaneous bacterial peritonitis,<sup>9–14</sup> and eventually, death. Furthermore, cirrhosis also confers a high risk of hepatocellular carcinoma (HCC)<sup>15</sup> and subsequent death.

There are strategies for temporal management of these complications, but it is not possible to reverse complicated cirrhosis without transplantation. In Japan, because of specific ethical considerations, deceased donor liver transplantation is extremely rare (average, about four cases per year in the entire country),<sup>16</sup> so 99% of liver transplants are living donor transplants from close relatives of the patients.<sup>17–20</sup> In Asia as in Western countries, there are fewer deceased donors than patients on the waiting list. Thus, the number of living donor liver transplantations (LDLT) is gradually increasing, as many patients and their families cannot wait for a cadaveric donor because their condition is life-threatening.<sup>21–28</sup>

Although liver transplantation is an effective treatment for patients with liver cirrhosis, there are some definite risks,<sup>29–41</sup> and some patients die prematurely owing to complications of liver transplantation. Thus, it is important to be able to predict precisely the natural course of liver cirrhosis and to compare the risks and benefits of liver transplantation with those of the natural disease course. In particular, for patients and families who have the option of LDLT, the timing should be given careful consideration because it can be controlled. Thus, candidate donors can afford to think about the risks they might face,<sup>42–44</sup> and from the patients' point of view, proper timing increases the success rate of the procedure.

The Model for End-Stage Liver Disease (MELD) score was first reported to be an objective score useful

for predicting patient survival after a transjugular intrahepatic portosystemic shunt (TIPS) procedure performed to relieve the complications of portal hypertension. MELD score is based on objective parameters: total bilirubin (T.Bil.), prothrombin time, international normalized ratio (PT-INR), and serum creatinine.<sup>45</sup> MELD score is preferable to the conventional Child-Pugh-Turcotte score,<sup>46-48</sup> which includes control of ascites and the grade of hepatic encephalopathy but which is assessed somewhat subjective.

MELD score is now widely used in Western countries to determine the prognosis of patients with cirrhosis,<sup>42,49-52</sup> and the United Network of Organ Sharing (UNOS) uses MELD score to determine which patients should have priority for receiving an organ from a deceased donor.<sup>53</sup> However, details of patient survival, for example, how long a patient with a particular MELD score can be expected to live, are not yet clear.

We conducted a study to determine whether MELD score can be used as a precise, objective marker to predict survival of patients with cirrhosis. We are particularly interested in predicting long-term survival of such patients, because this information is important when selecting patients who will benefit from liver transplantation and in the decision making surrounding the option of LDLT. We also compared the predicted natural survival of cirrhosis patients with the survival of patients who underwent LDLT to find the discriminative score, when the benefit of liver transplantation exceeded that of allowing the liver cirrhosis to follow its natural course.

## Patients and methods

### Patients

A total of 79 patients with cirrhosis diagnosed by abdominal computed tomography or ultrasound were included in this study. Imaging criteria for the diagnosis of cirrhosis included an irregular surface and intrahepatic density of the liver with or without abdominal collateral vessels, splenomegaly, or ascites. These patients were divided into two groups: those who died of hepatic failure due to liver cirrhosis ( $n = 33$ ), and those with Child class B or C liver cirrhosis who were followed up and survived for at least 24 months at our institute and related hospitals ( $n = 46$ ). The patients' characteristics are shown in Table 1. We included some patients who had HCC but whose main cause of death was hepatic failure, not the progression of HCC.

Thirty patients (22 men and 8 women) who underwent LDLT in our institute for liver cirrhosis between January 2003 and December 2006 were included as

**Table 1.** Patient characteristics

	Not transplanted	Transplanted
<i>n</i>	79	30
Age	57 (29-69)	57 (25-62)
M/F	48/31	22/8
Etiology		
HCV	43	14
HBV	14	11
NBNC	22	5
PT-INR	1.54 ± 0.44	1.75 ± 0.52
T.Bil. (mg/dl)	2.72 ± 2.06	5.00 ± 6.71
Albumin (g/dl)	3.04 ± 0.53	2.97 ± 0.49
CPT score	9 (5-13)	10 (7-14)
MELD score	14.3 ± 4.6	17.7 ± 7.0

HCV, hepatitis C virus; HBV, hepatitis B virus; NBNC, non-B non-C; PT-INR, prothrombin time, international normalized ratio; T.Bil., total bilirubin; CPT, Child-Pugh-Turcotte; MELD, Model for End-Stage Liver Disease

control subjects. Transplanted patients' etiologies are also shown in Table 1.

### MELD score

MELD scores were calculated as follows, according to the UNOS database:

$$\text{MELD score (UNOS current version)} = 9.57 \times \log_{10}(\text{creatinine (mg/dl)}) + 3.78 \times \log_{10}(\text{T.Bil. (mg/dl)}) + 11.20 \times \log_{10}(\text{PT-INR}) + 6.43$$

Creatinine >4 was automatically calculated as 4, and values <1 were automatically calculated as 1. Patients' data were obtained monthly, including MELD scores.

### Statistical analysis

To analyze the natural survival of the patients with cirrhosis and that of those who underwent liver transplantation, the Kaplan-Meier method was used, and the log-rank test was used to compare survival on the basis of MELD scores.  $P < 0.05$  was considered statistically significant. All analyses were done with StatView ver. 5.0.

## Results

### Significant stratification of survival of patients with cirrhosis according to MELD scores

We first investigated whether the survival of patients with cirrhosis could be stratified according to MELD score. The cirrhosis patients included in this study were divided into four groups according to the MELD score ranges (<12, 12-14, 15-18, >18). Patient survival differed significantly among these four groups ( $P = 0.0018$ , Fig. 1). These results showed the usefulness of the MELD

score for predicting the intermediate-term survival of patients with liver cirrhosis.

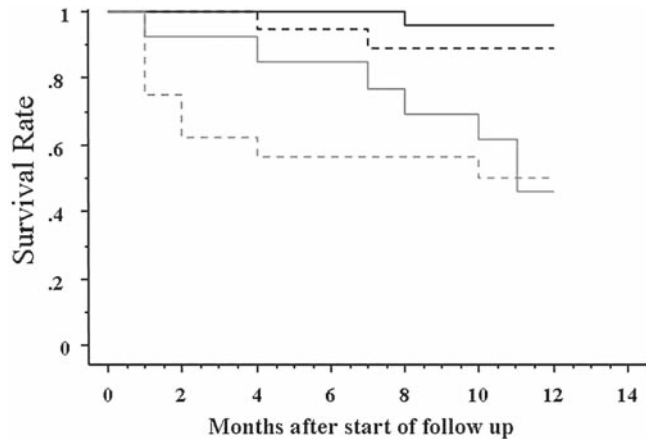
*Comparison of survival between patients with cirrhosis and those who underwent LDLT because of liver cirrhosis*

To determine whether a specific MELD score can predict a benefit of liver transplantation for patients with cirrhosis, we compared survival of the patients who

underwent LDLT with that of the cirrhosis patients who did not undergo liver transplantation in the four MELD score groups (Fig. 2).

Survival after LDLT was worse than that of nontransplanted cirrhosis patients for MELD scores of <12 and 12–15 (Fig. 2A,  $P = 0.2535$ ; Fig. 2B,  $P = 0.0314$ , respectively), and better than that for MELD scores of 15–18 or >18 (Fig. 2C,  $P = 0.1242$ ; Fig. 2D;  $P = 0.1365$ ), but the difference was not statistically significant except for patients with MELD scores of 12–15.

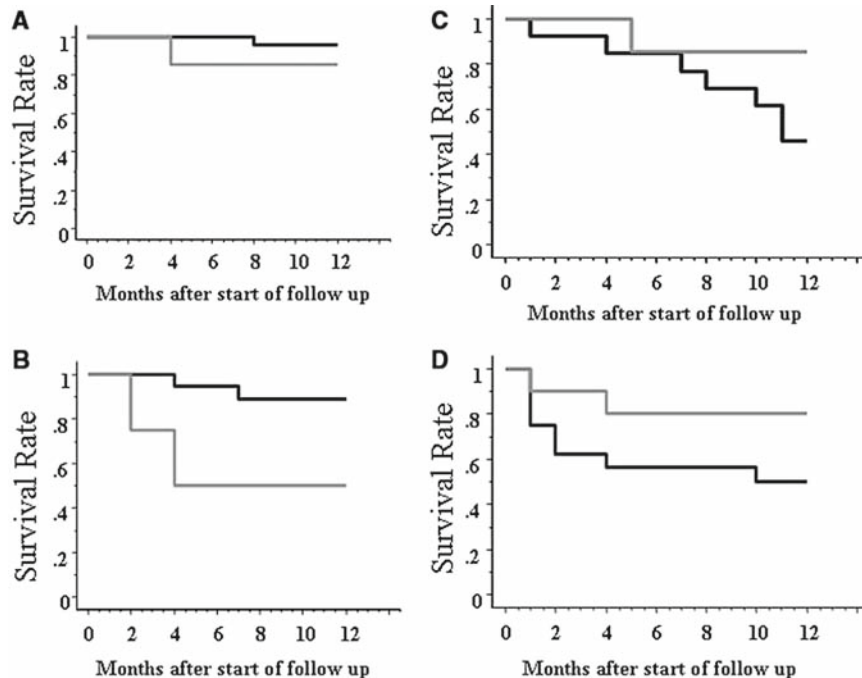
Therefore, we divided the nontransplanted patients into two groups according to whether their MELD score was <15 or  $\geq 15$ . We then found a statistically significant benefit of LDLT in comparison with nontransplanted patients with MELD scores of  $\geq 15$  (Fig. 3B,  $P = 0.0181$ ). In contrast, LDLT was associated with a significant risk in comparison with those with MELD scores of <15 (Fig. 3A,  $P = 0.0168$ ) compared with the cirrhosis patients whose disease followed its natural course. These results suggest that a MELD score of 15 can be used to discriminate whether the benefit of living donor transplantation outweighs the risk in patients with hepatic failure due to liver cirrhosis.



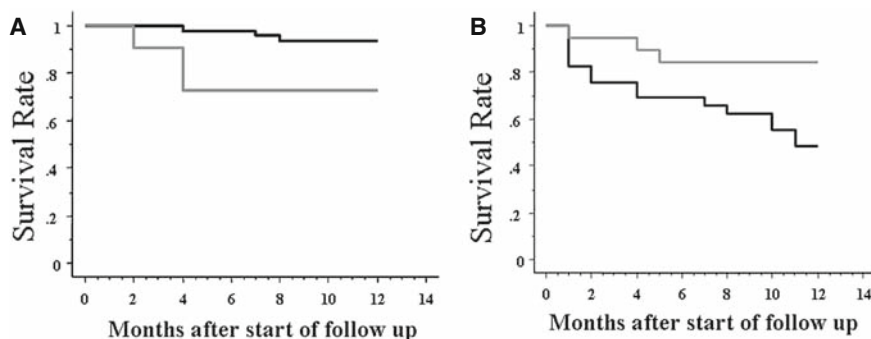
**Fig. 1.** Actual survival of patients with liver cirrhosis according to the Model for End-Stage Liver Disease (MELD) score category at the start of follow-up (black line, MELD score <12; black dashed line, MELD score 12–15; gray line, MELD score 15–18; gray dashed line, MELD score >18)

**Discussion**

Predicting the survival of patients with cirrhosis is important because these patients might be candidates for an important treatment option: liver transplantation. However, transplantation is not always fully suc-



**Fig. 2A–D.** Comparison between survival after living donor liver transplant (LDLT) and that in nontransplanted cirrhosis patients included in this study. **A** MELD score <12, not significant (NS); **B** MELD score 12–15, NS; **C** MELD score 15–18, NS; **D** MELD score  $\geq 18$ , NS. Black lines represent the survival of patients included in this study whose disease followed its natural course; gray lines represent the survival of patients receiving LDLT



**Fig. 3A, B.** Comparison between survival after LDLT and that of nontransplanted cirrhosis patients included in this study. **A** MELD score <15,  $P = 0.0232$ ; **B** MELD score  $\geq 15$ ,  $P = 0.0181$ ). *Black lines* represent the survival of patients whose disease followed its natural course; *gray lines* represent the survival of patients with LDLT

cessful, because of adverse effects or complications after transplantation. The reported 1-year survival rate is 70%–80%.<sup>29–41</sup> Therefore, the benefit of this treatment for any given patient must be clear so that transplantation can be used with maximum effect.

We selected the MELD score as an objective measure to predict survival of patients with cirrhosis. The Child-Pugh-Turcotte score is used universally to characterize the severity of liver cirrhosis and has the advantage of being very easy to use. It is an excellent score for evaluating liver function, including both synthetic and excretion functions, serum albumin, total bilirubin, and prothrombin time. However, because it also takes into account the severity of ascites and hepatic encephalopathy, it is somewhat subjective.

Other studies have compared the usefulness of the MELD score with that of the Child-Pugh-Turcotte score in predicting survival of patients with cirrhosis.<sup>54,55</sup> In this study, we focused on MELD score and analyzed the survival of patients with cirrhosis in detail. In previous studies, MELD score was shown to predict survival up to 1 year.<sup>48,54,56</sup> Our study not only confirmed these previously reported findings but also provided more detailed survival data.

In this study, MELD scores were shown to be particularly useful for predicting 1-year survival. If a candidate donor has a strong desire to help the patient, and this candidate has no medical problems, then living donor transplantation may be a treatment option. However, the surgery is not without risks to the donor,<sup>43,44</sup> and a few donors even die.<sup>52</sup> Therefore, when LDLT is being considered, both the family members and the patient must be well informed about the risks. In this context, precise prediction of the benefit of liver transplantation becomes important. Thus, its discriminative value makes the MELD score a powerful clinical tool not only for determining the prognosis of patients with cirrhosis but also the appropriate timing for the treatment choice of LDLT.

For a MELD score of <15, we showed that there are significant risks associated with transplantation compared with that of the natural disease course in cirrhosis

patients. However, in this study, only 1-year survival was compared, and much longer survival was not investigated. Also, if the main indication for transplantation is HCC, the risk might be evaluated differently. Therefore, we showed only a benefit of transplantation in patients with MELD score  $\geq 15$ , and a significant risk in 1-year survival in those with MELD score <15. Indications for transplantation should be considered case by case, and transplantation should not be completely denied to patients with MELD score <15.

Our study had some important limitations. It was retrospective, and although it was a multicenter study, the number of centers was small. In addition, there was an uneven distribution of patients in the groups; fewer patients had high MELD scores. This imbalance is unavoidable but it could be minimized by conducting a prospective, multicenter study to confirm our data.

In conclusion, we showed that the MELD score is an objective, easy-to-determine score that can predict intermediate-term survival of patients with liver cirrhosis. We also showed that the MELD score has clear value for discriminating between the risk of death in patients with cirrhosis and when they are likely to receive a significant benefit from liver transplantation. The MELD score can thus be used as a powerful tool to assist physicians and patients and their families in their decision making regarding liver transplantation, especially living donor liver transplantation.

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