Use of MELD Score in Country with Low Organ Donation

Somchai Limsrichamrern MD*, Prawej Mahawithitwong MD*,
Yongyut Sirivatanauksorn MD*, Pairoj Mitmanochai MD*

* Division of General Surgery, Department of Surgery, Faculty of Medicine Siriraj Hospital,
Mahidol University, Bangkok, Thailand

Background: The model for end-stage liver disease (MELD) score was used to prioritize liver allocation in the USA that decreased the mortality in awaiting patients. The current national policy for liver allocation in Thailand is to offer organs to the transplant center, not directly to the patients themselves. The aim of the present study was to determine the accuracy of MELD score to predict the mortality of patients on liver transplantation waiting list in Thailand, a country with low organ donation.

Material and Method: Between January 2006 and March 2007, we prospectively collected data of all patients on liver transplantation waiting list. MELD score was calculated. All patients were followed until they were transplanted, dead, or to the end of the present study. Patients were then divided into three groups (dead, alive, and transplanted) according to the outcome. Differences between groups were compared using Chi-square test.

Results: Seventy-three patients were enrolled (male:female = 48:25). Mean age was 55.6 years. At the end of the study, 44 patients were alive (60.3%, MELD 8-31), 21 were dead (28.8%, MELD 15-40), and eight were transplanted (11%, MELD 12-30). The dead group was compared with alive group to determine mortality. Patients who died had higher MELD score than patients who were alive. Patients with MELD score more than 15 had significantly (p-value = 0.006) higher mortality than patients with MELD score of less than 15.

Conclusion: MELD score is very useful in stratifying severity and mortality risk of cirrhotic patients while on liver transplant waiting list. A MELD score of 15 is associated with significantly increased mortality on awaiting patients. MELD score should be used to prioritize liver organ in order to save lives.

Keywords: Liver transplantation, Organ allocation, MELD score, Waiting list mortality

Liver transplantation is the treatment of choice for most patients with irreversible liver disease from a variety of acute and chronic etiologies. The success of liver transplantation has led to an increase in the number of patients referred for transplantation[1]. The number of transplants performed has not kept up with the growing number of individuals listed. This has led to substantial mortality in patients awaiting liver transplantation[2].

Liver allocation policy in the USA has gone through many stages of evolution. In February 2002, the United Network for Organ Sharing (UNOS) adopted the model for end-stage liver disease (MELD) score as the new policy to assess the disease severity and to determine priorities in deceased donor liver allocation[3]. The introduction of the MELD system resulted in a 12% decrease in the waiting list registrations, particularly for MELD values lower than 10 in the United States[4].

In Thailand, liver transplantation was first performed in 1987[5]. Between 2002 and 2005, there were more than 50 liver transplantations at Siriraj Hospital. However, the current national policy for liver organ allocation in Thailand is by offering organs to the transplant center, not to the patients themselves[6]. Each transplant program then develops its own allocation policy.

The authors proposed a hypothesis to evaluate the predictive value of MELD score for the death on waiting lists for liver transplantation candidates and survival analysis at a single center, Siriraj Hospital, between January 2006 and March 2007.

Material and Method

This study was approved by Siriraj's Ethic Committee before commencement of the study.

Correspondence to:

Limsrichamrern S, Division of General Surgery, Department of Surgery Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand.
Phone: 0-2419-8006
E-mail: somchai.lim@mahidol.ac.th

Study population

All patients on liver transplantation waiting lists at Siriraj hospital.

Inclusion criteria

All adult patients with chronic liver disease and hepatic malignancy who are candidates for liver transplantation following NIH criteria.

Exclusion criteria

- Fulminant hepatic failure
- Retransplantaion
- Non-cirrhotic, metabolic disorder of liver i.e. primary oxaluria or familial amyloidosis polyneuropathy.

All patients had complete data required for MELD score calculation at the time of listing and follow-up every three months between January 2006 and March 2007 until liver transplantation, the death occurred, or the end of observation. At the end of the present study, transplanted patients were excluded. The dead group was compared with the alive group to determine mortality and survival analysis.

The MELD score was calculated using the UNOS formula as followed:

MELD score = $10 \times \{[0.957 \times Log_e(Cr)]+[0.378 \times Log_e(Bilirubin)]+[1.120 \times Log_e(INR)]+0.643\}$

- Serum creatinine and bilirubin (mg/dl).
- The maximum serum creatinine considered within the MELD score equation will be 4.0 mg/dl (i.e., for patients with a serum creatinine of greater than 4.0 mg/dl, the serum creatinine level will be set to 4.0 mg/dl). For patients on dialysis, defined as having 2 or more dialysis treatments within the prior week, the serum creatinine level will automatically be set to 4.0 mg/dl.
- Laboratory values less than 1.0 will be set to 1.0 for the purposes of the MELD score calculation.
- The MELD score will be limited to a total of 40 points maximum.

In the patients with hepatocellular carcinoma (HCC), a MELD score of 22 was considered.

Statistical analysis

The analyses were performed using SPSS 11.5 software. Demographic data values were given as mean ± SD, frequency, and percentage. Student's t-test was used to compare between mean and SD of the alive and dead group. Pearson Chi-squares test was used for frequency comparison. The concordance (c-statistic) equivalent to the area under the receiver-operating characteristic curve (ROC) was measured to access the ability of MELD score to correctly stratify patients according to risk of death while on the waiting lists. The Kaplan-Meier method was used to calculate survival probabilities. A p-value of 0.05 or lower was considered significant.

Results

Seventy-three patients were enrolled (48 men, 25 women) with a mean age of 55.6 years (range 20 to 72 years). The patient characteristics are given in Table 1.

MELD score at the time of registry (18.35±6.5, range 6-31) and at the end of study (21.82±8.03, range 8 to 40) were compared in alive and death group. Patients who died had significantly higher MELD score at the time of registry and at the end of the study than patients who were the alive (p-value 0.003, <0.001). No patients with MELD score less than 15 died while on the waiting list. On the other hand, patients with MELD score ≥15 had significantly (p-value = 0.006) higher mortality than patients with MELD score <15. The ROC analysis performed for MELD score revealed an excellent predictive value for death (area = 0.83) as given in Fig. 1. MELD score at the end of the study was used to evaluate the mortality on the waiting list.

Eight patients were transplanted and were excluded from the analysis. Thus, sixty-five patients (44 alive, 21 dead) were analyzed. Baseline and follow-up data was shown in Table 2.

For further analysis, the authors used MELD score cut point of 15 at the time of registry to determine

Table 1. Demographic data of all patients

	Patient population (n = 73)
Male:female ratio	1.8:1
Age (year)	55.6±9.9
Status	
Alive	44 (60.3%)
Dead	21 (28.8%)
Transplant	8 (11.0%)
Blood group	
A	26 (35.6%)
B	18 (24.7%)
AB	5 (6.8%)
O	24 (32.9%)
MELD score (at the time of registry)	18.3±6.6 (6-31)
MELD score (at the end of study)	21.8±7.8 (8-40)

MELD = model for end-stage liver disease

Table 2. Demographic data of the selected 65 patients

	Selected group (n = 65)		p-value
	Alive (n = 44)	Dead (n = 21)	
Age (yr)	56.16±9.3 (range 21-72)	54.48±11.4 (range 20-69)	0.529
Sex			0.284
Male (n = 42)	26	16	
Female (n = 23)	18	5	
Blood group			0.582
A (n = 24)	15	9	
B (n = 16)	10	6	
AB (n = 2)	1	1	
O (n = 23)	18	5	
MELD score			
At the time of registry	16.73±6.2 (range 6-28)	21.76±5.7 (range 8-31)	0.003
At the end of study	18.50±5.6 (range 8-31)	28.76±8.0 (range 15-40)	<0.001

Table 3. Numbers of divided group

	Selected group (n = 65)		p-value
	Alive (n = 44)	Dead (n = 21)	
MELD score at registry			0.089
<15 (n = 20)	17	3	
≥15 (n = 45)	27	18	

Table 4. Time of follow-up until the end of the study

	Follow-up time	
	Mean (week)	Median (week)
Alive (n = 44)	50.26±17.9	58.21
Dead (n = 21)	21.97±19.7	22.86
Total (n = 65)	41.12±22.7	48.57

survival. Two groups showed no significant difference in number of patients as shown in Table 3. Median follow-up time for the whole group was 41.12 weeks (95% CI 1.29-91.14) and the detail was given in Table 4. Patients who had MELD score ≥15 at the time of registry had significantly lower survival than patients with MELD score <15 (p-value = 0.038, P75 = 25.7 week) (Fig. 2).

Discussion

In the past, UNOS used UNOS status to stratify patients for liver organ allocation. Problems with UNOS status was that it divided patients into four categories. There are many patients within the same status and patients in the same UNOS status can vary in severity of disease significantly. Waiting time was used to break tie. Patients who were transplanted might
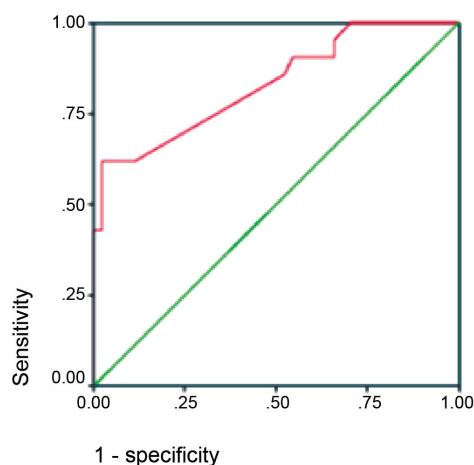

Fig. 1 ROC curve for MELD score as a predictor of death on waiting lists.
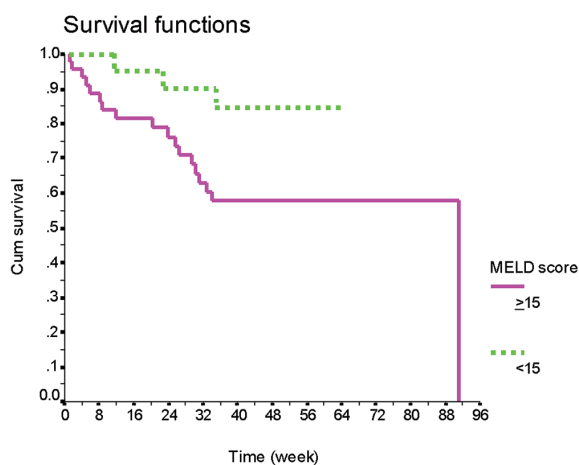

Fig. 2 Kaplan-Meier survival curve on liver transplantation waiting lists.

not be the sickest of the group. As a result, significant number of patients died while waiting for liver.

MELD score was developed by studying factors that predict mortality of patients with chronic liver disease[3]. Many variables were studied but only three were found to accurately predict mortality. Using mathematical analysis, the MELD score was developed which has been proved to predict progression of liver disease. By using MELD score for organ allocation, one would be able to allocate organ to the patient at highest risk of death, which theoretically would save the most lives.

UNOS adopted the model for end-stage liver disease (MELD) score as the new policy to determine priorities in deceased donor liver allocation in 2002. Many reports proved MELD score as an objective, reliable, and clinically useful model for assessing disease severity and predicting survival in patients with chronic liver disease. On the other hand, a report from Argentina showed increased waiting list mortality after adoption of MELD score[7].

In our single transplant center experience, MELD score had an excellent predictive value for death (area ROC = 0.83), which is similar to Gheorghe's study[8]. Patients who died had higher MELD score than patients who were alive. Patients with MELD score more than 15 had significantly (p-value = 0.006) higher mortality and lower survival (p-value = 0.038) than patients with MELD score of less than 15. Thus, MELD score of 15 can be used as a cut point for transplantation. Patients with MELD score greater than 15 should be transplanted as soon as possible to save their lives. On the other hand, patients with MELD score lower than 15 can be managed medically while on the transplant waiting list and forsake the liver organ to a sicker patient.

Organ donation rate are much lower in Thailand than that in USA[9]. To the author's knowledge, there have been no reports of the use of MELD score in prioritizing liver organ allocation in a country with organ donation rate less than two per million populations. The Organ Donation Center of Thai Red Cross Society allocates liver organs by offering liver to the transplant center that is on top of the list[6]. After the center receives the liver organ, that center will become the last on the list. That center will move up the list as the higher-on-the-list receives liver organ until it becomes top of the list again. Liver organs are not offered to the patients directly. With this allocation system, liver organ may not be offered to the sickest patient and waiting time for patients at a different center can vary considerably depending on how many patients the center has. The center that has a large number of patients on the waiting list will have a longer waiting time and higher mortality on waiting list as a consequence. On the other hand, a center with few patients on the waiting list will receive liver offer frequently and transplant to patient who may not be sick enough to get survival benefit from liver transplantation.

Our data has demonstrated a high mortality rate on the waiting list. The maximum time of follow-up was only 64.71 weeks, which may limit the ability to evaluate the long-term survival of patients on the waiting list. Measures to increase liver organ donation are required to reduce the waiting list mortality. Until organ donation promotion becomes fruitful, a center with a large number of patients on the waiting list will continue to have a high waiting list mortality. Measure to alleviate the waiting list mortality is to adjust allocation policy to offer liver organ to a sicker patient. Our data confirmed previous data that liver transplantation should be offered to patients with MELD score of 15 or higher. This recommendation holds true in a country with organ donation rate less than two per million populations.

Conclusion

MELD score is very useful in stratifying severity and mortality risk of cirrhotic patients while on the liver transplant waiting list. A MELD score of 15 is associated with significantly increased mortality on awaiting patients. In order to save lives, a MELD score cut point of 15 should be used as the appropriate indication for liver transplantation.

Potential conflicts of interest

None.

References

1. Farmer DG, Amersi F, Busuttil RW. Orthotopic liver transplantation. In: Blumgart LH, Fong Y, editors. Surgery of the liver and biliary tract. 3rd ed. Philadelphia: W.B. Saunders; 2000: 2071-85.
2. Wang VS, Saab S. Liver transplantation in the era of model for end-stage liver disease. Liver Int 2004; 24: 1-8.
3. Kamath PS, Wiesner RH, Malinchoc M, Kremers W, Therneau TM, Kosberg CL, et al. A model to predict survival in patients with end-stage liver disease. Hepatology 2001; 33: 464-70.
4. Freeman RB, Wiesner RH, Edwards E, Harper A,

Merion R, Wolfe R. Results of the first year of the new liver allocation plan. Liver Transpl 2004; 10: 7-15.

5. Sriwatanawongsa V, Sangsubhan C, Tanprayoon T, Borirakchanyavat V, Kyokong O, Vajarapongse K, et al. The first human orthotopic liver transplant in Thailand: a case report. Chula Med J 1988; 32: 463-468.

6. Organ Donation Center, The Thai Red Cross Society [Internet]. 2002 [cited 2013 Jan 13]. Available from: http://www.organdonate.in.th/wp-content/uploads/2012/07/method_2545.pdf

7. McCormack L, Gadano A, Lendoire J, Imventarza O, Andriani O, Gil O, et al. Model for end-stage liver disease-based allocation system for liver transplantation in Argentina: does it work outside the United States? HPB (Oxford) 2010; 12: 456-64.

8. Gheorghe L, Popescu I, Iacob R, Iacob S, Gheorghe C. Predictors of death on the waiting list for liver transplantation characterized by a long waiting time. Transpl Int 2005; 18: 572-6.

9. Global Observatory on Donation and Transplantation [Internet]. 2006 [cited 2013 Jan 13]. Available from: http://www.transplant-observatory.org/pages/Facts.aspx

---

การใช้ค่า *MELD score* ในผู้ป่วยรอการปลูกถ่ายอวัยวะตับในประเทศที่มีอัตราการบริจาคอวัยวะต่ำ

สมชัย ลิ้มศรีจำเริญ, ประเวชย์ มหาวิทิตวงศ์, ยงยุทธ ศิริวัฒนอักษร, ไพโรจน์ มิตรมโนชัย

ภูมิหลัง: การผ่าตัดปลูกถ่ายตับเป็นการรักษาที่ได้รับการยอมรับโดยทั่วไป ในประเทศสหรัฐอเมริกาได้มีการใช้ *model for end-stage liver disease (MELD) score* ในการจัดสรรอวัยวะตับให้แก่ผู้ป่วยที่รอรับการผ่าตัด และพบว่าสามารถลดอัตราการตายระหว่างรอของผู้ป่วยที่รอรับการผ่าตัดได้ สำหรับประเทศไทย ศูนย์รับบริจาคอวัยวะ สภากาชาดไทย ใช้วิธีการจัดสรรโดยจัดสรรอวัยวะตับให้แก่โรงพยาบาล มิได้จัดสรรให้แก่ผู้ป่วยโดยตรง จุดประสงค์ของการศึกษานี้คือ การศึกษาความแม่นยำของ *MELD score* ในการทำนายความเสี่ยงของการเสียชีวิตขณะรออวัยวะ

วัสดุและวิธีการ: การศึกษานี้ทำการศึกษาแบบไปข้างหน้าตั้งแต่ มกราคม พ.ศ. 2549 ถึง มีนาคม พ.ศ. 2550 ในผู้ป่วยทุกรายที่รอการผ่าตัดปลูกถ่ายอวัยวะตับที่โรงพยาบาลศิริราช ผู้ป่วยได้รับการติดตามจนกว่าจะได้รับการผ่าตัดปลูกถ่ายตับ หรือ จนกระทั่งเสียชีวิต หรือ จนสิ้นสุดการศึกษา หลังจากนั้นผู้ป่วยจะถูกแบ่งเป็น 3 กลุ่ม คือ กลุ่มที่เสียชีวิต กลุ่มที่ได้รับการผ่าตัด และกลุ่มที่มีชีวิตอยู่จนสิ้นสุดการศึกษา ตามผลลัพท์ที่เกิดขึ้น ความแตกต่างของแต่ละกลุ่มนำมาเปรียบเทียบกันเพื่อหาความแตกต่างทางสถิติ

ผลการศึกษา: ผู้ป่วย 73 ราย เข้าร่วมในการศึกษานี้ (เพศชาย 48 ราย เพศหญิง 25 ราย) อายุเฉลี่ยของผู้ป่วยเท่ากับ 55.6 ปี เมื่อสิ้นสุดการศึกษาพบว่าผู้ป่วย 44 ราย (60.3%) ยังชีวิตอยู่ (MELD 8-31) ผู้ป่วย 21 ราย (28.8%) เสียชีวิต (MELD 15-40) ผู้ป่วย 8 ราย (11%) ได้รับการผ่าตัดปลูกถ่ายอวัยวะตับ (MELD 12-30) กลุ่มผู้ป่วยที่เสียชีวิตมีค่า *MELD score* สูงกว่ากลุ่มที่มีชีวิตรอดอย่างมีนัยสำคัญ ผู้ป่วยที่มี *MELD score* มากกว่าหรือเท่ากับ 15 มีความเสี่ยงต่อการเสียชีวิตมากกว่าผู้ป่วยที่มี *MELD score* ต่ำกว่า 15 อย่างมีนัยสำคัญ (*p-value = 0.006*)

สรุป: *MELD score* เป็นเครื่องมือที่มีประโยชน์มากในการบ่งบอกความรุนแรงและความเสี่ยงต่อการเสียชีวิตในผู้ป่วยโรคตับแข็งที่รอการผ่าตัดปลูกถ่ายอวัยวะตับ ผู้ป่วยที่มีค่า *MELD score* เท่ากับ 15 หรือสูงกว่ามีความเสี่ยงต่อการเสียชีวิตขณะรออวัยวะตับ การจัดสรรอวัยวะตับควรใช้ *MELD score* ในการจัดสรรเพื่อรักษาชีวิตผู้ป่วยให้ได้มากที่สุด