J Korean Med Sci. 2023 Sep 4;38(35):e274
https://doi.org/10.3346/jkms.2023.38.e274
eISSN 1598-6357·pISSN 1011-8934

JKMS

Original Article
Cell Therapy & Organ Transplantation

Predicted Impact of the Model for End-Stage Liver Disease 3.0 in a Region Suffering Severe Organ Shortage

Deok-Gie Kim, Seung Hyuk Yim, Eun-Ki Min, Mun Chae Choi, Jae Geun Lee, Myoung Soo Kim, and Dong Jin Joo

Department of Surgery, The Research Institute for Transplantation, Yonsei University College of Medicine, Seoul, Korea

Received: Jan 19, 2023
Accepted: Apr 27, 2023
Published online: Aug 16, 2023

Address for Correspondence:
Dong Jin Joo, MD, PhD, FACS
Department of Surgery, The Research Institute for Transplantation, Yonsei University College of Medicine, 50-1 Yonsei-ro, Seodaemun-gu, Seoul 03722, Korea.
Email: djjoo@yuhs.ac

ORCID iDs
Deok-Gie Kim
https://orcid.org/0000-0001-9653-926X
Seung Hyuk Yim
https://orcid.org/0000-0003-2146-3592
Eun-Ki Min
https://orcid.org/0000-0003-3255-1942
Mun Chae Choi
https://orcid.org/0000-0002-2708-0755
Jae Geun Lee
https://orcid.org/0000-0002-6722-0257
Myoung Soo Kim
https://orcid.org/0000-0002-8975-8381
Dong Jin Joo
https://orcid.org/0000-0001-8405-1531

ABSTRACT

Background: The model for end-stage liver disease 3.0 (MELD3.0) is expected to address the flaws of the current allocation system for deceased donor liver transplantation (DDLT). We aimed to validate MELD3.0 in the Korean population where living donor liver transplantation is predominant due to organ shortages.
Methods: Korean large-volume single-centric waitlist data were merged with the Korean Network for Organ Sharing (KONOS) data. The 90-day mortality was compared between MELD and MELD3.0 using the C-index in 2,353 eligible patients registered for liver transplantation. Patient numbers and outcomes were compared based on changes in KONOS-MELD categorization using MELD3.0. Possible gains in MELD points and reduced waitlist mortality were analyzed.
Results: MELD3.0 performed better than MELD (C-index 0.893 for MELD3.0 vs. 0.889 for MELD). When stratified according to the KONOS-MELD categories, 15.9% of the total patients and 35.2% of the deceased patients were up-categorized using MELD3.0 versus MELD categories. The mean gain of MELD points was higher in women (2.6 ± 2.1) than men (2.1 ± 1.9, $P < 0.001$), and higher in patients with severe ascites (3.3 ± 1.8) than in controls (1.9 ± 1.8, $P < 0.001$); however, this trend was not significant when the MELD score was higher than 30. When the possible increase in DDLT chance was calculated via up-categorizing using MELD3.0, reducible waitlist mortality was 2.7%.
Conclusion: MELD3.0 could predict better waitlist mortality than MELD; however, the merit for women and patients with severe ascites is uncertain, and reduced waitlist mortality from implementing MELD3.0 is limited in regions suffering from organ shortage, as in Korea.

Keywords: MELD3.0; Liver Transplantation; Allocation; MELD; Waitlist Mortality

INTRODUCTION

The model for end-stage liver disease (MELD) is a tool developed for organ allocation in deceased donor liver transplantation (DDLT) based on predicted mortality.[1] MELD has been used worldwide since it was adopted by United Network for Organ Sharing (UNOS) as an

Disclosure
The authors have no potential conflicts of interest to disclose.

Author Contributions
Conceptualization: Kim DG, Joo DJ. Data curation: Min EK, Choi MC. Formal analysis: Kim DG, Yim SH. Investigation: Yim SH, Min EK, Lee JG, Kim MS, Joo DJ. Methodology: Kim DG. Supervision: Joo DJ. Writing - original draft: Kim DG, Yim SH. Writing - review & editing: Kim DG.

organ allocation policy in 2002. In 2016, UNOS reapplied the score, which added Na to the existing MELD as a liver allocation policy, thereby reducing waiting mortality and increasing the equity of organ use.[2,3] However, the accuracy of the MELD score for predicting waitlist mortality has been questioned due to recent changes in the characteristics and improvement in treatment of end-stage liver disease.[4] In addition, disparities in liver allocation between sexes has been reported in several countries due to overestimated kidney function in women.[5] Moreover, there is a need to consider liver failure complications such as ascites and encephalopathy, which are difficult to objectify. Reflecting this situation, Kim et al.[6] developed MELD3.0, which reflects the relationship between sex and the mortality of low albumin due to ascites. They reviewed its applicability, but no study has assessed its accuracy across the diversity of liver transplant (LT) circumstances in various countries.[6,7]

Korea applied the MELD allocation system in June 2016, which resulted in reduced waitlist mortality from 57.4 to 52.7 deaths per 100 person-years.[8] However, Korea suffers from a more severe organ shortage than Western countries, with 7.62 brain-dead liver donations per 1 million people per year.[9] As of 2020, 61% of Korean DDLTs have been performed in patients with an emergency status of 1 or MELD ≥ 38.[10] To overcome this organ shortage, living donor liver transplantation (LDLT) is predominant in Korea, with 74.4% of total liver transplantations performed with living donors in 2020.[11] This study thus attempted to validate the applicability of MELD3.0 to reduce LT waitlist mortality in Korea.

METHODS

Study population and data source

We performed a retrospective observational study with data from patients who were registered for the approval of LT between June 2005 and December 2021 at Severance Hospital, Korea. The patient list, demographics, and date of death or LT were retrieved from Korean Network for Organ Sharing (KONOS) and merged with institutional data on laboratory results that were necessary for the calculation of MELD and MELD3.0. Exclusion criteria were as follows: 1) age < 18 years at the first waitlisting, 2) prior organ transplantation history or waitlisting for LT, 3) listed for multiorgan transplantation other than liver and kidney, and 4) missing data. Although patients with hepatocellular carcinoma (HCC) fulfilling the Milan criteria received additional MELD points (+4 for MELD ≤ 13, +5 for MELD 14–20, and being assigned 25 points for MELD 21–25) after the MELD era, we did not exclude these patients because additional MELD points might not considerably affect the rate of DDLT in Korea, where patients with MELD < 25 had a very low possibility of DDLT.[12] Finally, 2,353 eligible patients were included in the analysis (**Supplementary Fig. 1**).

MELD and MELD3.0

The current allocation of deceased donor livers was performed with MELD, and we compared the predictive value for mortality and possible impact on the waiting list of MELD3.0 with MELD, without considering MELD-Na. MELD and MELD3.0 were calculated according to a previous study.[6]

$$\text{MELD} = 9.57 \times \log(\text{Cr}) + 3.78 \times \log(\text{bilirubin}) + 11.20 \times \log(\text{INR}) + 6.43$$

$$\begin{aligned}\text{MELD3.0} = {} & 1.33\ (\text{if woman}) + \{4.56 \times \log(\text{T.bil})\} + \{0.82 \times (137 - \text{Na})\} - \\ & \{0.24 \times (137\text{-Na}) \times \log(\text{T.bil})\} + \{9.09 \times \log(\text{INR})\} + \{11.14 \times \log(\text{Cr})\} + \\ & \{1.85 \times (3.5 - \text{Alb})\} - \{1.83 \times (3.5 - \text{Alb}) \times \log(\text{Cr})\} + 6\end{aligned}$$

https://doi.org/10.3346/jkms.2023.38.e274

where Cr is creatinine, INR is international normalized ratio, T.bil is total bilirubin, and Alb is albumin.

MELD point alteration by MELD3.0

Point alteration from MELD to MELD3.0 was depicted using a heatmap. Patients were grouped by MELD point ranges in line with the KONOS emergency grading, according to MELD and MELD3.0 separately: MELD ≤ 20 (KONOS grade 5), MELD 21–30 (KONOS grade 4), MELD 31–37 (KONOS grade 3), and MELD ≥ 38 (KONOS grade 2).

To evaluate the implications of MELD3.0, which improves the underestimation of disease severity in women and patients with severe ascites, we compared the mean gain of MELD points according to sex and the existence of severe ascites stratified by MELD groups. Severe ascites was defined as identification on imaging studies requiring diuretics or paracentesis.

Outcomes within 90 days of waitlisting

The primary endpoint was mortality within 90 days of the initial waitlisting. Patients were censored at the time of LT or removed from the waitlist due to causes other than death. The secondary endpoint was DDLT rate within 90 days. To evaluate mortality, we used the entire cohort, including pre- and post-MELD eras, and patients who received LDLT. In contrast, to analyze the DDLT rate, we only used a sub-cohort consisted of post-MELD era excluding patients who received LDLT to analyze possible impact of MELD point gain by MELD3.0 on wait-list.

Statistical methods

Mortality during the 90 days after waitlisting was evaluated using a Kaplan–Meier curve with the log-rank test, stratified by the MELD and MELD3.0 groups. Model performance for mortality was compared between MELD and MELD3.0 by calculating Harrel's C index with a test of statistical difference.[13] In addition, predictive powers for 90-day mortality of MELD and MELD3.0 were evaluated with calibration plots, which were constructed by smoothing curves from the observed and predicted risk of deaths per decile. The mean gain of points by using MELD3.0 was compared with the Student's *t*-test.

To estimate the possible impact of MELD3.0 on the waitlist, we calculated reducible waitlist mortality by the method previously suggested by Kim et al.[2] using a sub-cohort of patients who were wait-listed during post-MELD era and did not received LDLT within 90 days. First, the possible increased number of LT was calculated with following formula: $\sum\{(P_B - P_A) * N_{B-A}\}$, the sum of multiplying the difference of DDLT likelihood between different MELD3.0 strata, within the same MELD strata ($P_B - P_A$), and the number of deceased patients up-categorized by MELD3.0 (N_{B-A}). The results from the formula was divided by the number of total 90-day mortality was regarded as reducible wait-list mortality by MELD3.0. All analyses were performed using R statistical package, version 4.2.0, for macOS (http://cran.r-project.org), and statistical significance was set at $P < 0.05$.

Ethics statement

This study was performed in accordance with the Declaration of Helsinki and the Declaration of Istanbul and was approved by the Institutional Review Board (IRB) at Severance Hospital, Yonsei University Health System (IRB No.4-2022-0913). Informed consent was waived because of the retrospective nature of the study.

https://doi.org/10.3346/jkms.2023.38.e274

JKMS

RESULTS

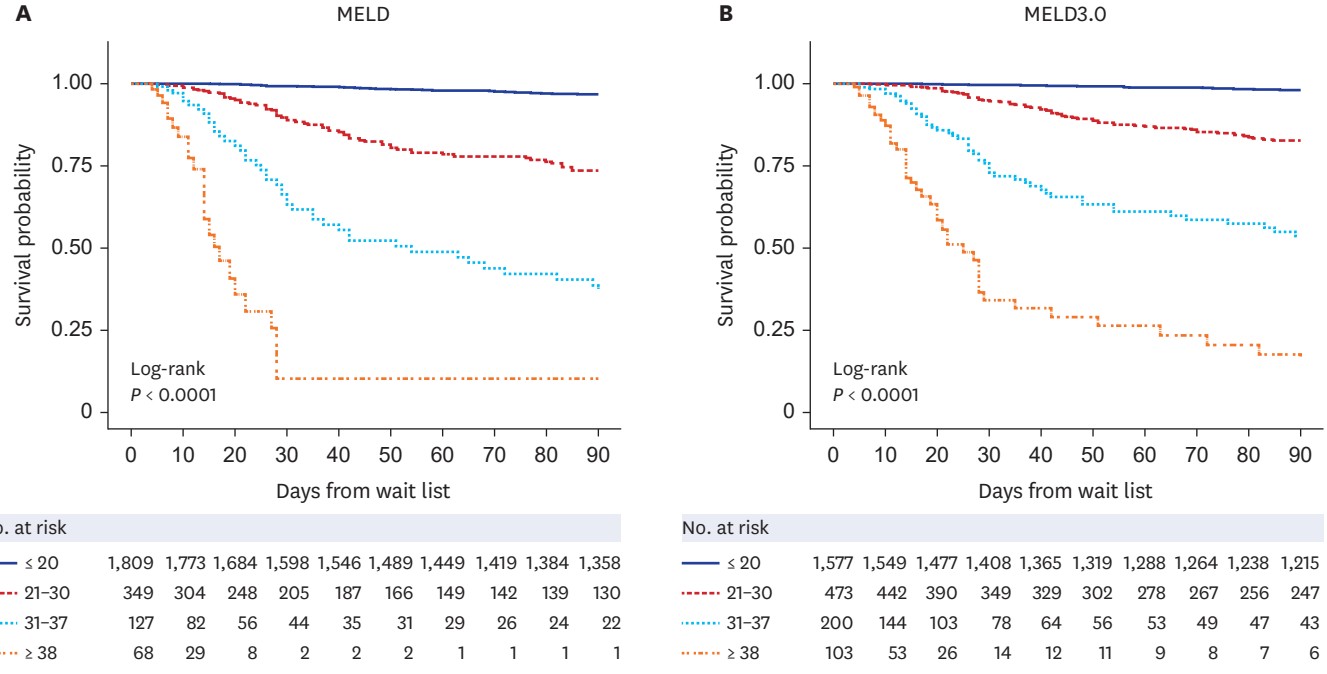
Characteristics of the study population

As shown in **Supplementary Table 1**, among the 2,353 eligible patients, 1,441 (60.0%) and 942 (40.0%) were waitlisted for LT before (2005.06–2016.05) and after MELD scoring was implemented (2016.06–2021.12). The median age was 55 (interquartile range [IQR], 46–61) years, and 652 (27.7%) patients were woman. HCC (n = 1,083, 46%) was the most common diagnosis for waitlisting, followed by alcoholic liver disease (n = 417, 17.7%) and hepatitis B virus (n = 413, 17.6%). Fifty-three (2.3%) patients were diagnosed with acute hepatitis. Severe ascites was observed in 544 patients (23.1%), and the median MELD score was 12 (IQR, 8–20). When categorized by the KONOS emergency grade, 1,809 (76.9%) had MELD scores ≤ 20, 349 (14.8%) had MELD scores 21–30, 127 (5.4%) had MELD scores 31–37, and 68 (2.9%) had MELD scores ≥ 38.

Within 90 days of the first waitlisting, 1,507 (64.0%) patients survived without LT, 490 (20.8%) received LDLT, 164 (7.0%) received DDLT, 179 (7.6%) died without LT, and 13 (0.6%) dropped out from the waitlist (**Supplementary Table 2**). Underlying liver diseases in patients who received LDLT and waited DDLT were provided in **Supplementary Table 3**.

Survival curve and model performance

In the Kaplan–Meier curve analyses, LT-censored 90-day survival rates were 96.6%, 73.5%, 36.9%, and 10.3% in the MELD ≤ 20, MELD 21–30, MELD 31–37, and MELD ≥ 38 groups, respectively ($P < 0.001$; **Fig. 1**). When stratified by MELD3.0 score, LT-censored 90-day survival rates were 97.4%, 77.9%, 45.5%, and 9.1% in the MELD3.0 ≤ 20, MELD3.0 21–30, MELD3.0 31–37, and MELD3.0 ≥ 38 group, respectively ($P < 0.001$).



No. at risk										
≤ 20	1,809	1,773	1,684	1,598	1,546	1,489	1,449	1,419	1,384	1,358
21–30	349	304	248	205	187	166	149	142	139	130
31–37	127	82	56	44	35	31	29	26	24	22
≥ 38	68	29	8	2	2	2	1	1	1	1

No. at risk										
≤ 20	1,577	1,549	1,477	1,408	1,365	1,319	1,288	1,264	1,238	1,215
21–30	473	442	390	349	329	302	278	267	256	247
31–37	200	144	103	78	64	56	53	49	47	43
≥ 38	103	53	26	14	12	11	9	8	7	6

Fig. 1. Kaplan–Meier curve analyses for 90-day mortality after first liver transplantation waitlisting. (**A**) MELD and (**B**) MELD3.0 groups.
MELD = model for end-stage liver disease.

https://doi.org/10.3346/jkms.2023.38.e274

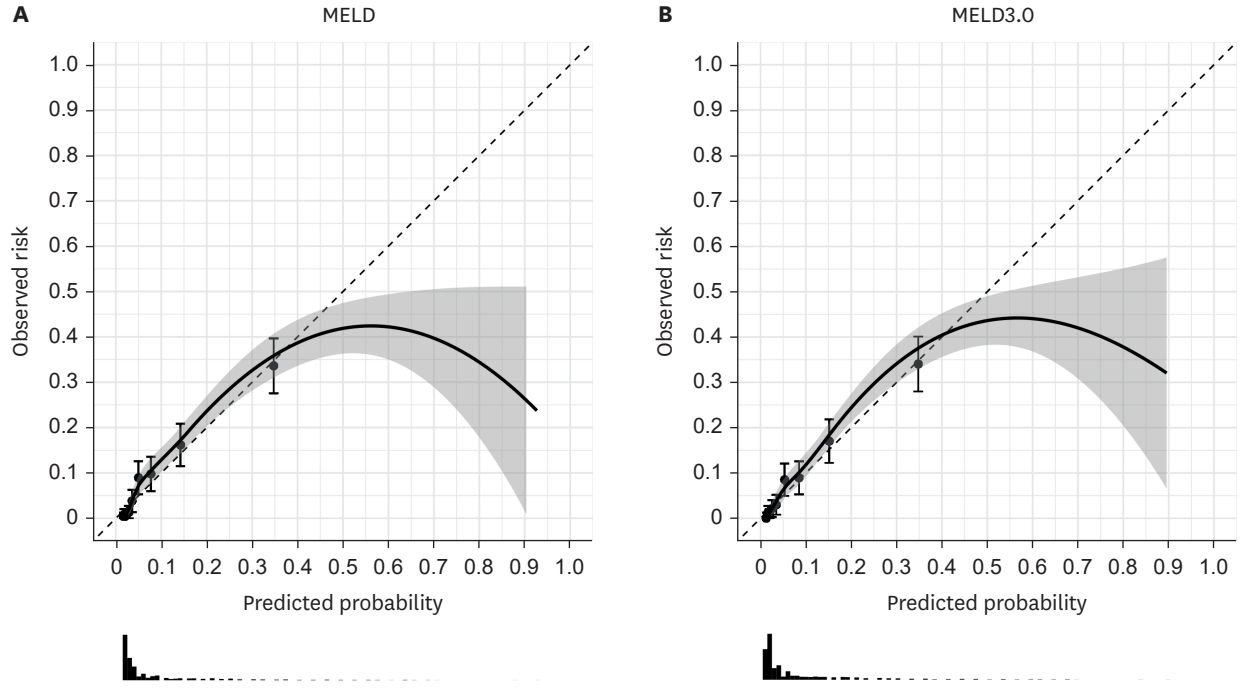


Fig. 2. Calibration plot for 90-day mortality. (**A**) MELD and (**B**) MELD3.0 groups. Calibration of the predicted and observed risk of 90-day mortality is presented per decile of the population. The diagonal line represents the exact prediction.
MELD = model for end-stage liver disease.

The predicted mortality and corresponding observed risk for 90-day mortality according to MELD and MELD3.0 scores are depicted as a calibration plot in **Fig. 2**. Both MELD and MELD3.0 scores showed good prediction of 90-day mortality in patients whose predicted risk was within the 9th centile, while mortality in the 10th centile was overestimated. The C-index for survival was moderately higher in MELD3.0 than in MELD: the difference was statistically significant (0.889 [95% CI, 0.865–0.912] for MELD and 0.893 [95% CI, 0.871–0.914] for MELD3.0; $P < 0.001$).

MELD3.0 re-categorization and 90-day mortality

Table 1 shows the distribution of patients and death according to MELD and MELD3.0 categories. Two-hundred thirty-two patients (9.9%) in the MELD ≤ 20, 108 patients (4.6%) in the MELD 21–30, and 35 patients (1.5%) in the MELD 31–37 groups were up-categorized by the MELD3.0 score. In total, 375 patients (15.9%) were up-categorized, and none were down-categorized using the MELD3.0 score.

Among the 179 patients who died within the study period, 63 (35.2%) were up-categorized: 24 were upgraded from MELD ≤ 20 to MELD3.0 21–30, 23 from MELD 21–30 to MELD3.0 31–37, and 16 from MELD 21–30 to MELD3.0 ≥ 38. Within MELD categories, cumulative 90-day mortalities were higher in up-categorized patients: 12.9% for the up-categorized group vs. 2.1% for the control group with MELD ≤ 20; 38.5% vs. 22.4% among patients whose MELD score was 21–30; and 78.4% vs. 56.2% among patients whose MELD score was 31–37. This flow of MELD group changes by MELD3.0 was provided as the diagram either (**Supplementary Fig. 2**).

https://doi.org/10.3346/jkms.2023.38.e274

Table 1. Distribution of patients according to MELD and MELD 3.0 group

MELD group	MELD 3.0 group				Total
	≤ 20	21–30	31–37	≥ 38	
Total patients					
≤ 20	1,577 (67.0%)	232 (9.9%)[a]			1,809 (76.9%)
21–30		241 (10.2%)	108 (4.6%)[a]		349 (14.8%)
31–37			92 (3.9%)	35 (1.5%)[a]	127 (5.4%)
≥ 38				68 (2.9%)	68 (2.9%)
Total	1,577 (67.0%)	473 (20.1%)	200 (8.5%)	103 (4.4%)	2,353 (100%)
Death					
≤ 20	28 (2.1%)	24 (12.9%)[a]			52 (3.4%)
21–30		37 (22.4%)	23 (38.5%)[a]		60 (26.5%)
31–37			27 (56.2%)	16 (78.4%)[a]	43 (63.1%)
≥ 38				24 (89.7%)	24 (89.7%)
Total	28 (2.1%)	61 (17.3%)	50 (46.3%)	40 (85.3%)	179

[a]Patients up-categorized by MELD 3.0. For death, data was presented as the number of deceased patients (cumulative mortality) within 90 days.
MELD = model for end-stage liver disease.

Table 2. The number and rate of DDLT within 90 days after wait-listing among patients except those who received LDLT during post-MELD era

MELD group	MELD 3.0 group				Total
	≤ 20	21–30	31–37	≥ 38	
≤ 20	2/442 (0.5%)	1/88 (1.1%)[a]			3/530 (0.6%)
21–30		10/75 (13.3%)	9/31 (29.0%)[a]		19/106 (17.9%)
31–37			13/31 (41.9%)	9/16 (56.2%)[a]	22/47 (46.8%)
≥ 38				21/32 (65.6%)	21/32 (65.6%)
Total	2/442 (0.5%)	11/163 (6.7%)	22/62 (35.5%)	30/48 (62.5%)	65/715 (9.1%)

[a]Patients up-categorized by MELD3.0. Post-MELD era indicated time since 2016.6.1. Data represents the numbers of DDLT/total patients prone to DDLT (rates of DDLT).
DDLT = deceased donor liver transplantation, LDLT = living donor liver transplantation, MELD = model for end-stage liver disease.

MELD3.0 re-categorization and DDLT rate

Table 2 shows DDLT rates up to 90 days after the initiation of MELD allocation system among patients except those who received LDLT within the study period. A total 65 of 715 (9.1%) patients received DDLT. Within same MELD category, the up-categorized patients received a higher rate of DDLT than those who remained in the same category; 1.1% for the up-categorized group vs. 0.5% for the control group among patients with MELD score ≤ 20; 29.0% vs. 13.3% among patients whose MELD score was 21–30; and 56.2% vs. 41.9% among patients whose MELD score was 31–37.

Effect of MELD3.0 on the waiting list

Change of MELD points by MELD3.0 was shown in **Fig. 3**. Among 2,353 patients, the mean gain of MELD points by MELD3.0 scoring was 2.2 ± 2 0. The number of patients who gained MELD points was 2,019 (85.8%), while 326 (13.9%) maintained the same MELD score. Eight patients lost MELD points by MELD3.0 scoring (0.3%). The maximum gain of points was 12. Characteristics among patients who gained MELD points and those who did not was provided as **Supplementary Table 4**.

When comparing MELD categories, the MELD 21–30 group showed the highest MELD point gain (3.4 ± 1.6; **Table 3**). Women gained more points than men (2.6 ± 2.1 for women vs. 2.1 ± 1.9 for men, respectively, $P < 0.001$). However, this trend was seen only in the MELD ≤ 20 group (2.4 ± 2.1 vs. 2.4 ± 2.0, $P < 0.001$), while men gained more points in the MELD 31–37 group (2.2 ± 1.3 vs. 3.0 ± 1.3, $P = 0.002$). The overall gain in MELD points was higher in patients with severe

https://doi.org/10.3346/jkms.2023.38.e274

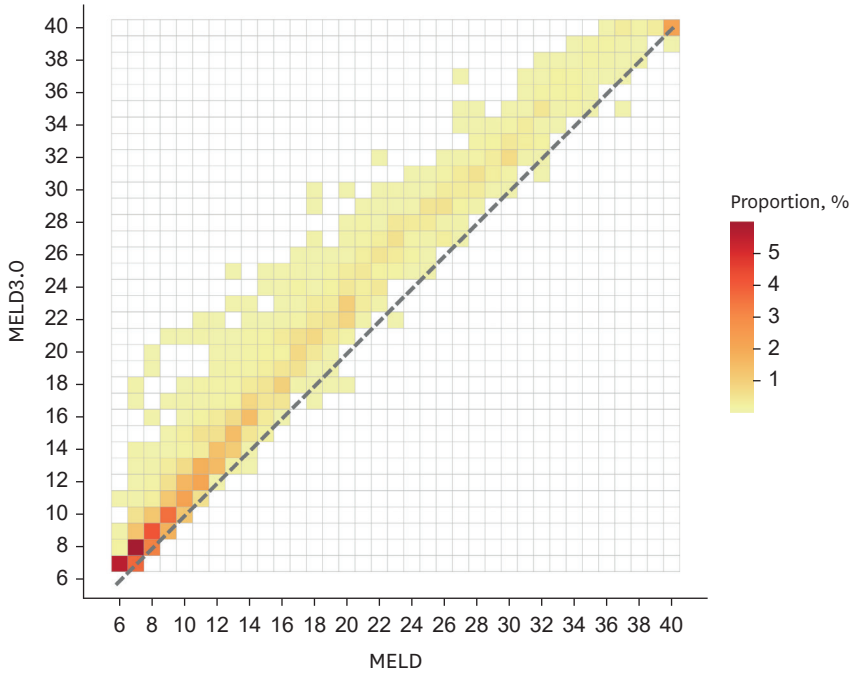


Fig. 3. Change of MELD points by MELD3.0. Diagonal means same points for original MELD and MELD3.0.

ascites (3.3 ± 2.3 vs. 1.9 ± 1.8); however, this trend was only seen in the MELD ≤ 20 (3.5 ± 2.5 vs. 1.7 ± 1.7, $P < 0.001$) and MELD 21–30 groups (3.7 ± 1.7 vs. 3.2 ± 1.5, $P = 0.013$).

We calculated reducible wait-list mortality using sub-cohort of post-MELD era according to the method previously described by Kim et al.[14] Among total 75 deceased patients, 22 were up-categorized by MELD3.0 and the possible increased number of LT was only two. This suggests MELD3.0 could reduce waitlist mortality by 2.7%. Detailed calculation process is provided in **Supplementary Table 5**.

DISCUSSION

This study validated the impact of MELD3.0 versus MELD using single-centric waitlist data in Korea, where LDLT is predominant due to severe organ shortages. Although both MELD and MELD3.0 reflected 90-day mortality accurately, MELD3.0 performed better (C-index 0.893 vs. 0.889, respectively). When stratified according to the KONOS-MELD categories, 15.9% of

Table 3. Mean gain of MELD points by MELD3.0

Variables	MELD ≤ 20		MELD 21–30		MELD 31–37		MELD ≥ 38	
	No.	Mean ± SD	No.	Mean ± SD	No.	Mean ± SD	No.	Mean ± SD
By MELD group, total	1,809	2.1 ± 2.0	349	3.4 ± 1.6	127	2.7 ± 1.4	68	0.2 ± 0.6
By sex[a]								
Women	469	2.4 ± 2.1	114	3.6 ± 1.8	49	2.2 ± 1.3	20	0.3 ± 0.6
Men	1,340	1.9 ± 2.0	235	3.3 ± 1.5	78	3.0 ± 1.3	48	0.0 ± 0.5
By severe ascites[b]								
Yes	337	3.5 ± 2.5	140	3.7 ± 1.7	40	2.6 ± 1.0	27	0.3 ± 0.7
No	1,472	1.7 ± 1.7	209	3.2 ± 1.5	87	2.7 ± 1.5	41	0.2 ± 0.5

Shadow means $P < 0.05$ for the difference between subgroups.
MELD = model for end-stage liver disease, SD = standard deviation.
[a]2.6 ± 2.1 for female vs. 2.1 ± 1.9 for male, $P < 0.001$; [b]3.3 ± 2.3 for patients with severe ascites vs. 1.9 ± 1.8 for those without, $P < 0.001$.

https://doi.org/10.3346/jkms.2023.38.e274

the total patients and 35.2% of the deceased patients were up-categorized using MELD3.0. When analyzed with a subgroup with MELD scores, the DDLT rate was higher in patients who were up-categorized by MELD3.0 than in the controls. Women gained more MELD points on average; however, this trend was observed only in patients with MELD < 20. In addition, the mean MELD score improved more in patients with severe ascites than in those without; however, this trend was seen only in those with a MELD score < 30. Compared to the current allocation system using MELD, the possible reduction in waitlist mortality by implementing MELD3.0 was 2.7%.

Korea has a very high rate of LDLT, i.e., up to 70% of total LT, owing to a severe organ shortage. MELD has been implemented since June 2016 in Korea for the efficient and fair allocation of deceased donor livers to end-stage liver disease patients without eligible living donors. Data from one year after implementation showed reduced waitlist mortality and improved regional equality.[8] However, most deceased donor livers were allocated to patients with high MELD (**Supplementary Fig. 3**). As the number of deceased donors have decreased recently, there is a greater need to improve the MELD allocation system. In contrast to the United States and many European countries, Korea has not yet implemented MELD-Na; thus, direct conversion to MELD3.0, which avoids the flaws of MELD, could be more efficient. This study provides good evidence for the adoption of MELD3.0 in countries similar to Korea.

In this study, MELD3.0 showed better 90-day mortality outcomes than MELD. Although 20% of the study population received LDLT, censoring at the time of LT might have improve the mortality associated with MELD3.0 implementation. Calibration plots showed that MELD3.0 was better than MELD; however, both models overestimated mortality at the upper end of the scale, similar to a MELD-Na validation study in Eurotransplant.[14] This may be due to the low number of participants with high MELD scores, as the scores from the first registration were used.

In contrast to the UNOS policy, which provides three MELD points for HCC patients based on the median MELD score of local recent LT recipients at the time of transplant, Korea gives MELD exception points only for current MELD scores below 25.[15] This makes a minimal difference, considering the median MELD for DDLT recipients in Korea. In addition, MELD and MELD3.0 were not registered in KONOS and were calculated from laboratory tests when the patient first entered the waitlisting. Thus, we included patients who received MELD exception points for HCC as they minimally affected the DDLT rate in our population.

MELD3.0 was modeled to supplement the sex disparity against women in organ allocation.[5] In this study, the mean gain in women from MELD3.0 scoring was higher, but only in patients with MELD ≤ 20; men with MELD scores 31–37 showed higher MELD gains than women. Another purpose of MELD3.0 is to reflect the presence of ascites via serum albumin: a factor in the Child-Pugh-Turcotte score-based allocation.[6] In our population, patients with severe ascites showed a two-fold MELD gain than the controls. However, no significant difference was observed in patients with a MELD score of ≥ 31. This could attribute to the nature of the formular for MELD3.0, which reflect the interaction between the components included.

In Korea, where most DDLTs are performed for patients with high MELD scores, movement from MELD to MELD3.0 might hardly be beneficial to women and patients with severe ascites.

We demonstrated a reduction of 90-day waitlist mortality by 2.7% with MELD3.0 implementation; this was lower than those obtained in the MELD-Na validation studies in

UNOS (7%) and Eurotransplant (4.9%).[14,15] This suggests that the MELD3.0 could perform better for waitlist mortality in Koreans, but the reduction in waitlist mortality could be lower than that in western countries. In addition to improving the allocation system, it is important to increase the deceased donor pool; thus, measures such as activation of organ donation, expansion of acceptable donor criteria,[16] and implementation of donation after cardiac deaths, which have not yet been actively performed in Korea,[17] could help. Furthermore, LDLT for patients with a high MELD score could be a good alternative in regions with severe organ shortages. A Korean single-center study reported comparable outcomes between LDLT and DDLT in patients with a high MELD score with acute-on-chronic liver failure.[18] The Hong Kong group also recently reported the survival benefit of LDLT in patients with MELD ≥ 25 via waitlist matched ITT approaches.[19] However, further studies are needed to assess the benefit of LDLT in patients with high MELD scores, including regional DDLT rates and waitlist mortality.

MELD is not only an important index for liver allocation but is also a powerful risk factor for survival after DDLT.[20] MELD3.0 could help allocate livers to patients with higher pre-surgical mortality risks, thus reducing waitlist mortality. However, it could also result in an overall increase in post-transplant deaths, especially in regions where a high MELD score is needed for liver allocation. This problem should be discussed when a new allocation policy is applied.

Single-centric data analysis is an important limitation of our study, as laboratory results for the calculation of MELD3.0 have not been mandatorily accumulated in the KONOS database. However, this is the first study to show the utility of MELD3.0 in Korea using data from a large-volume center. Our validation was based on MELD re-categorization using MELD3.0, not MELD-Na, because of the relatively late implementation of MELD in Korea. Although this was a limitation, our results can provide a good reference for countries still using MELD and considering the application of MELD3.0, such as Korea. Lastly, Korea has a different allocation system and donor pool than in the US where MELD3.0 was developed; thus, the interpretation of our analyses should be done with caution. Specific versions of the MELD model adapted to individual countries could provide more insight into each region.

This single-centric study showed that MELD3.0 scoring improved 90-day waitlist mortality to as low as 2.7%, when compared to MELD in regions with severe organ shortage and LDLT predominance. However, in situations where most DDLTs were performed in patients with high MELD scores, the merits for women and patients with severe ascites are uncertain. Further studies should be conducted using national waitlist data.

ACKNOWLEDGMENTS

The authors thank the members of the Organ Transplant Support Team at Severance Hospital for their support in performing this research.

SUPPLEMENTARY MATERIALS

Supplementary Table 1
Patient characteristics

Click here to view

Supplementary Table 2
Results within 90 days after first wait-listing

Click here to view

Supplementary Table 3
Underlying liver diseases in patients who received LDLT and waited DDLT

Click here to view

Supplementary Table 4
Comparison of characteristics among patients who gained MELD points and those who did not

Click here to view

Supplementary Table 5
Calculation of reducible wait-list mortality by MELD3.0 using post-MELD era sub-cohort

Click here to view

Supplementary Fig. 1
Study population.

Click here to view

Supplementary Fig. 2
Sankey diagram depicting flow of MELD group changes by MELD3.0.

Click here to view

Supplementary Fig. 3
Annual LT number in Korea.

Click here to view

REFERENCES

1. 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(2):464-70.
PUBMED | CROSSREF
2. Kim WR, Biggins SW, Kremers WK, Wiesner RH, Kamath PS, Benson JT, et al. Hyponatremia and mortality among patients on the liver-transplant waiting list. *N Engl J Med* 2008;359(10):1018-26.
PUBMED | CROSSREF
3. Nagai S, Chau LC, Schilke RE, Safwan M, Rizzari M, Collins K, et al. Effects of allocating livers for transplantation based on model for end-stage liver disease-sodium scores on patient outcomes. *Gastroenterology* 2018;155(5):1451-1462.e3.
PUBMED | CROSSREF
4. Godfrey EL, Malik TH, Lai JC, Mindikoglu AL, Galván NT, Cotton RT, et al. The decreasing predictive power of MELD in an era of changing etiology of liver disease. *Am J Transplant* 2019;19(12):3299-307.
PUBMED | CROSSREF

5. Locke JE, Shelton BA, Olthoff KM, Pomfret EA, Forde KA, Sawinski D, et al. Quantifying sex-based disparities in liver allocation. *JAMA Surg* 2020;155(7):e201129.
PUBMED | CROSSREF
6. Kim WR, Mannalithara A, Heimbach JK, Kamath PS, Asrani SK, Biggins SW, et al. MELD 3.0: the model for end-stage liver disease updated for the modern era. *Gastroenterology* 2021;161(6):1887-1895.e4.
PUBMED | CROSSREF
7. Goudsmit BF, Putter H, Van Hoek B. The model for end-stage liver disease 3.0: an update without proven accuracy. *Gastroenterology* 2022;162(6):1781-2.
PUBMED | CROSSREF
8. Lee J, Kim DG, Lee JY, Lee JG, Joo DJ, Kim SI, et al. Impact of model for end-stage liver disease score-based allocation system in Korea: a nationwide study. *Transplantation* 2019;103(12):2515-22.
PUBMED | CROSSREF
9. iRODAT Database. Worldwide liver transplant from deceased donors 2021 (PMP). https://www.irodat.org/?p=database. Accessed December 19, 2023.
10. 2020 Annual report of Korean Organ Transplantation Registry. https://www.kotry.org/ko/rang_board/list.html?code=old_report. Accessed December 19, 2023.
11. 2020 Annual report of Korean Network for Organ Sharing (KONOS). https://www.konos.go.kr/board/boardListPage.do?page=sub4_2_1&boardId=30. Accessed December 19, 2023.
12. Korea Disease Control and Prevention Agency, Korea National Institute of Health; Korean Society for Transplantation; Korean Organ Transplantation Registry. *2021 KOTRY Annual Data Report.* Cheongwon, Korea: Korea National Institute of Health; 2022, 59-60.
13. Harrell FE Jr, Califf RM, Pryor DB, Lee KL, Rosati RA. Evaluating the yield of medical tests. *JAMA* 1982;247(18):2543-6.
PUBMED | CROSSREF
14. Goudsmit BF, Putter H, Tushuizen ME, de Boer J, Vogelaar S, Alwayn IP, et al. Validation of the model for end-stage liver disease sodium (MELD-Na) score in the Eurotransplant region. *Am J Transplant* 2021;21(1):229-40.
PUBMED | CROSSREF
15. OPTN policies, 9.5 specific standardized MELD or PELD score exceptions. https://optn.transplant.hrsa.gov/media/eavh5bf3/optn_policies.pdf. Updated 2023. Accessed December 19, 2023.
16. Vodkin I, Kuo A. Extended criteria donors in liver transplantation. *Clin Liver Dis* 2017;21(2):289-301.
PUBMED | CROSSREF
17. Park H, Jung ES, Oh JS, Lee YM, Lee JM. Organ donation after controlled circulatory death (Maastricht classification III) following the withdrawal of life-sustaining treatment in Korea: a suggested guideline. *Korean J Transplant* 2021;35(2):71-6.
PUBMED | CROSSREF
18. Moon DB, Lee SG, Kang WH, Song GW, Jung DH, Park GC, et al. Adult living donor liver transplantation for acute-on-chronic liver failure in high-model for end-stage liver disease score patients. *Am J Transplant* 2017;17(7):1833-42.
PUBMED | CROSSREF
19. Wong TC, Fung JY, Pang HH, Leung CK, Li HF, Sin SL, et al. Analysis of survival benefits of living versus deceased donor liver transplant in high model for end-stage liver disease and hepatorenal syndrome. *Hepatology* 2021;73(6):2441-54.
PUBMED | CROSSREF
20. Roll GR, Spiro M, Raptis DA, Jalal A, Yan CT, Olthoff KM, et al. Which recipient pretransplant factors, such as MELD, renal function, sarcopenia, and recent sepsis influence suitability for and outcome after living donor liver transplantation? A systematic review of the literature and expert panel recommendations. *Clin Transplant* 2022;36(10):e14656.
PUBMED | CROSSREF