Application of model for end-stage liver disease as disease classification in cardiac valve surgery: a retrospective study based on the INSPIRE database

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Background: Model for end-stage liver disease (MELD) is an effective predictive marker for renal, hepatic, and cardiac dysfunctions. In this study, we explore the correlation between MELD scores and the outcomes of patients undergoing cardiac valve surgery.

Methods: We conducted a retrospective analysis of clinical data from patients who underwent cardiac valve surgery, encompassing procedures on the aortic valve, mitral valve, and tricuspid valve, using the Informative Surgical Patient dataset for Innovative Research Environment (INSPIRE) database, we conducted receiver operating characteristic (ROC) analyses on the study participants and chose MELD as the primary scoring tool for our study due to its optimal area under the curve (AUC), patients were stratified into high (MELD ≥18) and low (MELD <18) groups based on the determined cutoff value. The perioperative clinical data of the two groups were compared.

Results: The analysis revealed 751 patients in the low MELD group (75.5%) and 244 patients (24.5%) in the high MELD group. Patients in the high MELD group exhibited a lower body mass index (BMI) compared to those in the low MELD group. In comparison to the low MELD group, the high MELD group exhibited a higher rate of emergency surgery (10.66% *vs.* 5.99%, P=0.01), along with prolonged anesthesia time, surgery time, and cardiopulmonary bypass (CPB) time. Regarding clinical prognosis, the high MELD group demonstrated a higher 28-day mortality rate (10.66% *vs.* 0.8%, P<0.001), as also observed in the analysis of three valve subgroups. Additionally, the high MELD group experienced longer hospitalization and intensive care unit (ICU) stay, and a higher proportion of patients requiring mechanical circulatory support, including intra-aortic balloon pump (IABP) assist (14.75% *vs.* 3.86%, P<0.001), extracorporeal membrane oxygenation (ECMO) assist (7.38% *vs.* 0.8%, P<0.001), and continuous renal replacement therapy (CRRT) (27.87% *vs.* 1.46%, P<0.001) post-surgery. The Kaplan-Meier survival curves illustrated a significantly lower mortality rate in the low MELD group compared to the high MELD group, with highly significant statistical differences (P<0.001).

Conclusions: The MELD score demonstrates a robust predictive value for clinical outcomes following cardiac valve surgery, underscoring its utility as a viable metric for disease stratification research.

Keywords: Model for end-stage liver disease (MELD); disease classification; cardiac valve surgery

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Introduction

Over the past three decades, the primary gauge of hepatic dysfunction (HD) has been the Child-Turcotte-Pugh (CTP) classification (1). However, the CTP score incorporates subjective indicators, thereby limiting its applicability in medical studies. Recently, the model for end-stage liver disease (MELD) has emerged as the predominant scoring system for prioritizing patients on the liver transplantation waiting list. The MELD score, encompassing both liver and renal function, has become a widely used prognostic tool for individuals with liver disease (2). Calculated using baseline serum creatinine, serum total bilirubin, and international normalized ratio (INR) for prothrombin time, the MELD score, initially designed for end-stage liver disease patients, has also been proposed as an effective predictive marker for renal, hepatic, and cardiac dysfunctions (3,4).

The variables composing the MELD score serve as indicators of multisystem dysfunction and coagulopathy. They play a pivotal role in identifying individuals at an elevated risk of experiencing renal failure and right ventricular failure (5), particularly during the perioperative period of heart transplantation and aortic dissection (6-8).

Highlight box

Key findings

• Model for end-stage liver disease (MELD) score demonstrates a robust predictive value for clinical outcomes following cardiac valve surgery, underscoring its utility as a viable metric for disease stratification research.

What is known and what is new?

• MELD score serves as indicators of multisystem dysfunction and coagulopathy and play a pivotal role in identifying individuals at an elevated risk of experiencing renal failure and hepatic dysfunction, particularly during the perioperative period of heart transplantation and aortic dissection.

• In this study, we explore the correlation between MELD score and the outcomes of patients undergoing cardiac valve surgery.

What is the implication, and what should change now?

• MELD score plays an important predictive value in perioperative cardiac valve surgery and can effectively guide disease stratification. Dynamic MELD score during perioperative period may bring positive clinical results.

In this study, we explore the correlation between MELD scores and the outcomes of patients undergoing cardiac valve surgery. We present this article in accordance with the STROBE reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-242/rc).

Methods

Study design

We conducted a retrospective analysis of clinical data from patients who underwent cardiac valve surgery, encompassing procedures on the aortic valve, mitral valve, and tricuspid valve, using the Informative Surgical Patient dataset for Innovative Research Environment (INSPIRE) database (9). This database comprises records of all individuals undergoing systemic, intraspinal, and regional anesthesia surgeries at Seoul National University Hospital from January 2011 to December 2020. The study's inclusion criteria were as follows: (I) patients who underwent open-heart valve replacement surgery (aortic valve, mitral valve, tricuspid valve); (II) patients aged 18 years or older. Exclusion criteria were defined as: patients with incomplete clinical data. The flow chart illustrating the patient screening process is depicted in *Figure 1*. At the initiation of our study, the INSPIRE database contained a total of 99,900 patients with 126,754 hospitalizations. In our approach, the same patient with different admissions was considered as two cases, while the same hospitalization with multiple surgeries is considered as one case. After excluding patients who underwent non-heart valve replacement surgery and one patient with incomplete clinical data, our study included a total of 973 patients with 995 hospitalizations. This encompassed 596 patients with 602 admissions for aortic valve surgery, 331 patients with 340 admissions for mitral valve surgery, and 52 patients with 53 admissions for tricuspid valve surgery. There were 6 patients who had two different procedures in two hospitalizations, so they overlapped in the subgroup, so the sum was greater than the total above.

Ethical statement

Approval for this study was obtained from the Committee on Ethics of Biomedical Research at Shanghai East
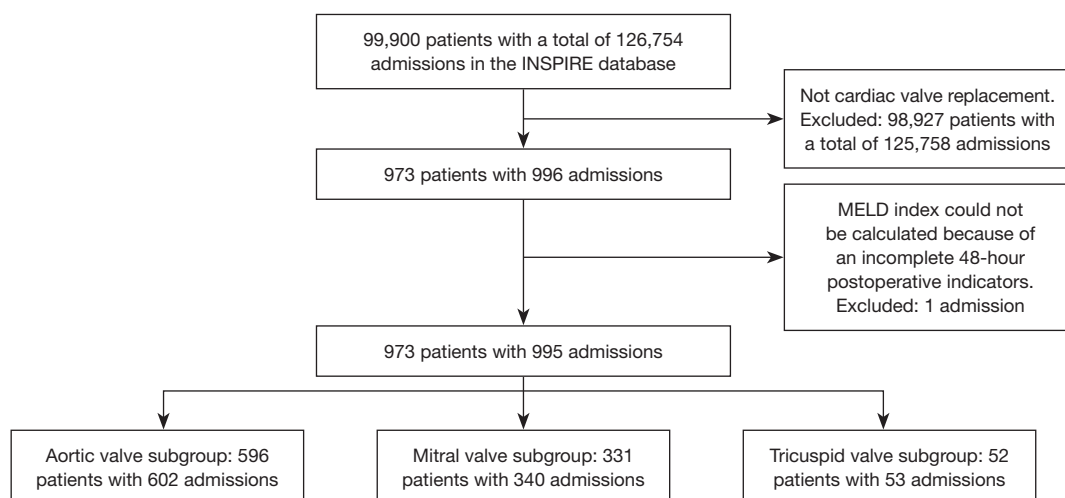
Figure 1 The flowchart of study. INSPIRE, Informative Surgical Patient dataset for Innovative Research Environment; MELD, model for end-stage liver disease.

Hospital, Tongji University School of Medicine, Shanghai (No. TJUSM2023-010), with a waiver for individual patient consent. This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

Data collection

We gathered comprehensive data on patients, encompassing demographic details such as age, sex, body mass index (BMI), and an array of laboratory test results including albumin, leukocytes, troponin, alanine transaminase (ALT), aspartate transaminase (AST), oxygen partial pressure (PaO$_2$), partial pressure of carbon dioxide (PaCO$_2$), base excess, C-reactive protein (CRP), among others. Surgical conditions, such as the method of anesthesia, emergency surgery status, operation time, extracorporeal circulation time, and more, were also documented as part of the study.

The postoperative clinical outcomes recorded included parameters such as postoperative 28-day mortality, occurrences of pneumonia, duration of stay in the intensive care unit (ICU), and the necessity for interventions like continuous renal replacement therapy (CRRT), extracorporeal membrane oxygenation (ECMO), intra-aortic balloon pump (IABP), and others.

Definitions and grouping

Currently, there exist various MELD scores and their modified versions, detailed as follows:

$$MELD = 11.2 \cdot \ln(INR) + 3.78 \cdot \ln(total\ bilirubin) + 9.75 \cdot \ln(creatinine) + 6.43 \quad [1]$$

$$MELD\text{-}Na = MELD + 1.32 \times (137 - sodium) - 0.033 \times MELD \times (137 - sodium) \quad [2]$$

$$\begin{aligned} MELD\ 3.0 = {}& 4.56 \cdot \ln(total\ bilirubin) + 0.82 \cdot (137 - sodium) \\ & - 0.24 \cdot (137 - sodium) \cdot \ln(total\ bilirubin) \\ & + 9.09 \cdot \ln(INR) + 11.14 \cdot \ln(creatinine) \\ & + 1.85 \cdot (3.5 - albumin) \\ & - 1.83 \cdot (3.5 - albumin) \cdot \ln(creatinine) + 6 \end{aligned} \quad [3]$$

$$MELD\text{-}X1 = 5.11 \cdot \ln(total\ bilirubin) + 11.76 \cdot \ln(creatinine) + 9.44 \quad [4]$$

These equations represent different formulations of the MELD score, each designed to assess liver function and predict outcomes in patients with liver disease.

We conducted receiver operating characteristic (ROC) analyses using the four scores on the study participants, and the specific results are depicted in *Figure 2*. Prognostic assessment and area under the curve (AUC) comparison of the four scores, MELD emerged as the primary scoring tool for our study due to its optimal AUC. Using the optimal cut-off point of 18 obtained from its ROC analysis, patients were categorized into two groups. Biochemical indicators (bilirubin, creatinine, INR) within 48 hours of admission to the ICU were utilized for scoring. Patients were then stratified into high (MELD ≥18) and low (MELD <18) groups based on the determined cutoff value. Subsequently, we conducted an in-depth analysis of the clinical baseline data and perioperative clinical prognosis outcomes for the two patient groups.
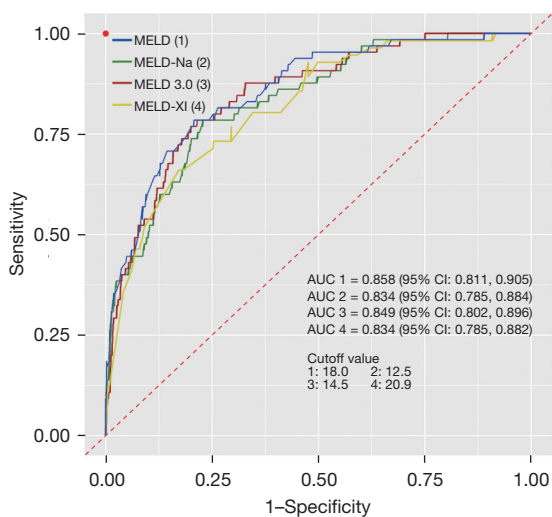
Figure 2 The ROC analyses of four scores. MELD, model for end-stage liver disease; AUC, area under the curve; ROC, receiver operating characteristic; CI, confidence interval.

Statistical analysis

All data were subjected to statistical analysis using Statistical Package for the Social Science (SPSS) 29.0 software. ROC curve was employed to determine the optimal critical value of the MELD score for predicting the prognosis of patients undergoing open cardiac valve surgery. Additionally, survival curves for the two patient groups were generated and analyzed. For normally distributed measurement data, values were presented as mean ± standard deviation, and comparisons were performed using independent sample t-tests. For non-normally distributed measurement data, a description was provided using quartiles [median (P_{25}, P_{75})], and statistical calculations were performed using non-parametric tests. Counting data were expressed as rates, and comparisons were conducted using χ^2 tests or Fisher's exact test, as appropriate. The overall survival rate between the two groups was calculated using the Kaplan-Meier method. A significance level of $P<0.05$ was used to denote statistical significance.

Results

Baseline demographic and clinical data of patients included in primary analysis

As previously outlined in the "definitions and grouping" section, MELD was chosen as the research indicator for grouping. The analysis revealed 751 patients in the low MELD group (75.5%) and 244 patients (24.5%) in the high

MELD group.

A comprehensive analysis of baseline data is presented in *Table 1*. Notably, patients in the high MELD group exhibited a lower BMI compared to those in the low MELD group. Statistically significant differences were observed in preoperative laboratory tests, including albumin, troponin, neutrophil percentage, platelet count, aspartate aminotransferase, activated partial thromboplastin time (APTT), urea nitrogen, CRP, and INR ($P<0.05$).

Intraoperative data and postoperative data between the groups

Intraoperative and postoperative data for the two groups included in the final analysis are compared in *Tables 2,3*. In comparison to the low MELD group, the high MELD group exhibited a higher rate of emergency surgery (10.66% *vs.* 5.99%, P=0.01), along with prolonged anesthesia time, surgery time, and cardiopulmonary bypass (CPB) time. Regarding clinical prognosis, the high MELD group demonstrated a higher 28-day mortality rate (10.66% *vs.* 0.8%, P<0.001), as also observed in the analysis of three valve subgroups. Additionally, the high MELD group experienced longer hospitalization and ICU stay, and a higher proportion of patients requiring mechanical circulatory support, including IABP assist (14.75% *vs.* 3.86%, P<0.001), ECMO assist (7.38% *vs.* 0.8%, P<0.001), and CRRT (27.87% *vs.* 1.46%, P<0.001) post-surgery. The postoperative laboratory test comparison outcomes were shown in Table S1.

Survival Kaplan-Meier survival curves

The Kaplan-Meier survival curves illustrated a significantly lower mortality rate in the low MELD group compared to the high MELD group, with highly significant statistical differences (P<0.001) evident in the results (*Figure 3*). ROC analysis of three different valves showed that cutoff (sensitivity: 0.706, specificity: 0.833) for aortic valve surgery was 18.2, AUC =0.831 [95% confidence interval (CI): 0.759, 0.903], cutoff (sensitivity: 0.760, specificity: 0.844) for mitral valve surgery was 19.4, AUC =0.875 (95% CI: 0.818, 0.933), and cutoff (sensitivity: 0.833, specificity: 0.979) for tricuspid valve surgery was 22.6, AUC =0.961 (95% CI: 0.900, 1.000) (cause of low mortality) (*Figure 4*).

Discussion

Cardiac valve surgery, a staple in managing heart valve diseases such as mitral and aortic valve stenosis, carries

Table 1 Preoperative baseline data of two groups of patients

Variables	All	MELD <18 group (n=751)	MELD ≥18 group (n=244)	Statistical value	P
Gender (male)	540 (54.27)	397 (52.86)	143 (58.61)	2.448	0.12
Age (years)	65 [55, 75]	65 [50, 70]	70 [60, 75]	4.960	<0.001
Weight (kg)	60 [51, 68]	60 [53, 68]	56 [49, 64.5]	−3.190	<0.001
Height (cm)	161 [154, 167]	160 [154, 167]	162 [154, 167]	0.098	0.92
BMI (kg/m^2)	23.0 [20.5, 25.3]	23.3 [21.0, 25.6]	21.7 [19.6, 24.4]	−5.010	<0.001
Albumin (g/dL)	3.9 [3.4, 4.2]	4.0 [3.6, 4.3]	3.5 [3.0, 4.1]	−5.320	<0.001
Troponin I (µg/L)	0.03 [0.01, 0.13]	0.02 [0.01, 0.06]	0.11 [0.03, 0.44]	5.045	<0.001
Fibrinogen (mg/dL)	302 [263, 360]	293 [263, 343]	314 [257, 360]	1.234	0.22
PO$_2$ (mmHg)	107 [92, 143]	107 [92, 143]	108 [92, 147]	1.237	0.22
PCO$_2$ (mmHg)	39.6 [37.0, 42.1]	40.0 [37.0, 42.5]	38.8 [36.0, 41.6]	−2.255	0.02
Base surplus (mmol/L)	0.4 [−0.9, 1.7]	0.4 [−0.9, 1.3]	0 [−1.5, 1.8]	−1.607	0.11
White blood cell count (/nL)	6.26 [4.71, 7.84]	6.26 [5.14, 7.62]	5.52 [4.19, 8.31]	−1.522	0.13
Neutrophil percentage (%)	63.0 [55.9, 72.6]	60.9 [52.9, 69.5]	67.4 [60.1, 77.7]	5.214	<0.001
Platelet count (/nL)	176 [134, 216]	198 [164, 231]	150 [114, 188]	−7.134	<0.001
Alanine aminotransferase (IU/L)	20 [13, 30]	20 [13, 28]	19 [12, 35]	0.249	0.80
Aspartate aminotransferase (IU/L)	25 [19, 35]	23 [18, 31]	31 [23, 49]	5.008	<0.001
APTT (s)	34.8 [31.2, 43.1]	33.8 [30.7, 38.4]	38.4 [33.0, 56.5]	5.191	<0.001
Urea nitrogen (mg/dL)	16 [13, 24]	15 [13, 20]	23.5 [15, 37]	7.579	<0.001
Creatine kinase (IU/L)	64 [47, 99]	64 [49, 99]	49.5 [39, 99]	−2.201	0.03
CRP (mg/dL)	0.19 [0.06, 1.64]	0.11 [0.06, 0.57]	0.78 [0.19, 4.60]	5.905	<0.001
INR	1.10 [1.00, 1.27]	1.05 [0.98, 1.19]	1.21 [1.08, 1.54]	6.098	<0.001
MELD	5.74 [2.83, 11.02]	4.67 [2.16, 7.96]	13.42 [8.68, 18.66]	13.468	<0.001

Data are presented as median [P25, P75] or n (%). MELD, model for end-stage liver disease; BMI, body mass index; PO$_2$, oxygen partial pressure; PCO$_2$, partial pressure of carbon dioxide; APTT, activated partial thromboplastin time; CRP, C-reactive protein; INR, international normalized ratio.

inherent risks of complications like renal and liver dysfunction (10,11). The MELD score emerges as a robust, non-invasive tool, leveraging accessible laboratory metrics for its computation. Its reliance on objective, non-respiratory parameters streamline its use in clinical settings, making it particularly invaluable in assessing perioperative liver function among cardiac surgery patients (12,13).

A previous study corroborates the utility of MELD for predicting liver dysfunction post-acute type A aortic dissection surgeries, with its early application facilitating the identification of at-risk patients (14). The score's sensitivity and effectiveness in disease stratification have been affirmed in coronary artery bypass and heart transplantation cases

(15-17). Our study extends these findings, demonstrating the efficacy of early MELD scoring post-heart valve surgery as a stratification tool. High preoperative levels of clinical indicators such as aspartate aminotransferase, APTT, urea nitrogen, CRP, and INR, in conjunction with extended surgical and CPB duration, are predictors of elevated postoperative MELD scores. Notably, patients with higher early postoperative scores typically face poorer prognoses, including higher in-hospital mortality rates and increased dependency on mechanical circulatory support and CRRT for acute kidney injury (AKI).

While the inclusion of INR as a coagulation indicator in the MELD score and the requirement for CPB assistance

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Table 2 Clinical data of the two groups during operation

Variables	All	MELD <18 group (n=751)	MELD ≥18 group (n=244)	Statistical value	P
Emergency operation	71 (7.14)	45 (5.99)	26 (10.66)	6.045	0.01
Duration of anesthesia (min)	425 [350, 510]	410 [340, 485]	467.5 [396, 599]	7.271	<0.001
Operating room time (min)	445 [370, 530]	435 [360, 510]	495 [420, 619]	7.311	<0.001
Operation time (min)	360 [285, 440]	345 [275, 420]	403 [335, 524]	7.397	<0.001
CPB time (min)	200 [160, 250]	195 [150, 240]	230 [185, 270]	7.362	<0.001
Invasive MAP (mmHg)	66 [64, 68]	66 [64, 68]	64 [60, 68]	−4.839	<0.001
BIS	37 [31, 41]	38 [33, 41]	35 [29, 40]	−4.972	<0.001
CI (L/min/m^2)	2.3 [2.0, 2.7]	2.3 [2.0, 2.7]	2.4 [2.0, 2.8]	1.443	0.15
CVP (mmHg)	6 [4, 7]	6 [2, 7]	6 [4, 7]	2.264	0.02
PEEP (cmH$_2$O)	0 [0, 2.5]	0.5 [0, 2.0]	0 [0, 3.0]	−0.425	0.67
Respiratory rate (/min)	11 [10, 12]	11 [10, 12]	11 [10, 12]	−1.341	0.18
Intraoperative tidal volume (mL)	432 [384, 472]	440 [384, 472]	424 [368, 472]	−1.957	0.05

Data are presented as median [P25, P75] or n (%). MELD, model for end-stage liver disease; CPB, cardiopulmonary bypass; MAP, mean arterial pressure; BIS, bispectral index score; CI, cardiac index; CVP, central venous pressure; PEEP, positive end-respiratory pressure.

Table 3 Clinical results of the two groups

Variables	All	MELD <18 group (n=751)	MELD ≥18 group (n=244)	Statistical value	P
In-hospital time (h)	432 [312, 672]	408 [312, 576]	600 [408, 1,002]	9.441	<0.001
ICU stay time (h)	48 [26, 97]	47 [25, 83]	100 [46, 170]	9.541	<0.001
Number of patients in subgroups					
Subgroup 1 (aortic valve)	602	480 (79.7)	122 (20.3)	–	–
Subgroup 2 (mitral valve)	340	239 (70.3)	101 (29.7)	–	–
Subgroup 3 (tricuspid valve)	53	32 (60.4)	21 (39.6)	–	–
Postoperative 28 d mortality	32 (3.22)	6 (0.8)	26 (10.66)	57.484	<0.001
Subgroup 1 (aortic valve)	15 (2.49)	3 (0.63)	12 (9.84)	33.969	<0.001
Subgroup 2 (mitral valve)	13 (3.82)	3 (1.26)	10 (9.9)	14.432	<0.001
Subgroup 3 (tricuspid valve)	4 (7.55)	0	4 (19.05)	6.593	0.01
Receiving reoperation	8 (0.8)	2 (0.27)	6 (2.46)	11.102	0.001
Receiving CRRT	79 (7.94)	11 (1.46)	68 (27.87)	175.661	<0.001
ECMO assist	24 (2.41)	6 (0.8)	18 (7.38)	33.855	<0.001
IABP assist	65 (6.53)	29 (3.86)	36 (14.75)	35.786	<0.001
Atrial fibrillation and flutter	46 (4.62)	32 (4.26)	14 (5.74)	0.911	0.34
Heart failure	12 (1.21)	8 (1.07)	4 (1.64)	0.509	0.48
Arterial embolism and thrombosis	1 (0.1)	1 (0.13)	0	0.325	0.57
Bacterial pneumonia, not elsewhere classified	1 (0.1)	1 (0.13)	0	0.325	0.57
Pneumonia, unspecified organism	5 (0.5)	4 (0.53)	1 (0.41)	0.056	0.81
Complications of cardiac and vascular prosthetic devices, implants and grafts	19 (1.91)	10 (1.33)	9 (3.69)	5.462	0.02

Data are presented as median [P25, P75] or n (%). MELD, model for end-stage liver disease; ICU, intensive care unit; CRRT, continuous renal replacement therapy; ECMO, extracorporeal membrane oxygenation; IABP, intra-aortic balloon pump.
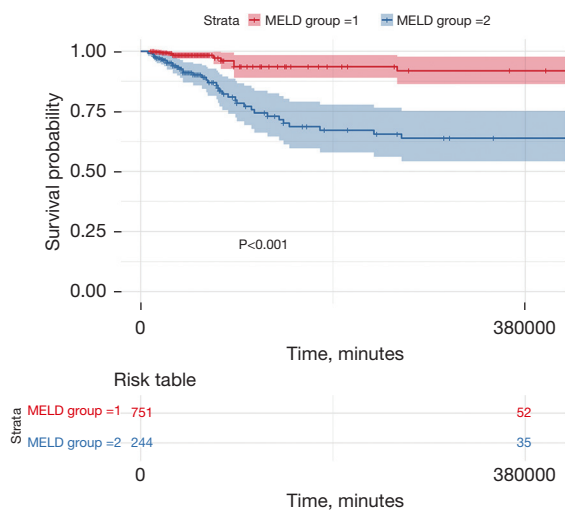
Figure 3 The Kaplan-Meier survival curves. MELD group =1: MELD <18 group; MELD group =2: MELD ≥18 group. MELD, model for end-stage liver disease.
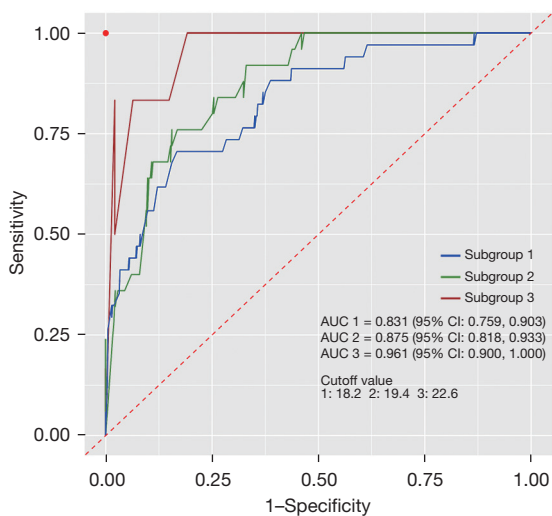
Figure 4 ROC analysis of three different valves—subgroup 1: aortic valve group; subgroup 2: mitral valve group; subgroup 3: tricuspid valve group. AUC, area under the curve; ROC, receiver operating characteristic; CI, confidence interval.

during smooth heart valve surgery have some impact on the score. Although previous studies have suggested that MELD-XI may have better practical applications (15), our research has found that MELD is more suitable in this type of surgery. Our study not only highlights the diagnostic value of the MELD score but also demonstrates its superiority over the MELD-XI and other modified MELD

scores in predicting mortality risk. This may be attributed to the fact that all our scores were evaluated within 48 hours after surgery, which eliminates the impact of postoperative warfarin anticoagulation on INR. However, further research is needed to confirm this. The underlying mechanism is that venous congestion and hyperthyroidism can contribute to elevated liver enzymes and other factors, leading to cardiovascular renal hepatic syndrome (18). The progression of liver dysfunction in patients with acute hepatic failure (AHF) is complex and may follow various paths.

The optimal MELD threshold for cardiac surgery has historically been debated, with previous literature advocating for a 14–15 range (19,20). Contrarily, our analysis supports a threshold of 18, balancing sensitivity and specificity to avoid diluting disease stratification efficacy. It is pertinent to consider variable thresholds across different surgical interventions. The assessment of organ function becomes paramount for patients with multiple preoperative risks undergoing complex procedures. The MELD score, thus, serves as a critical barometer for clinical guidance, highlighting patients necessitating focused care to potentially enhance clinical outcomes. In conclusion, while the MELD score is a valuable prognostic tool for postoperative complications, it is incumbent upon us to refine its application post-heart valve surgery through continued research, aiming to optimize patient prognosis.

Limitations

This study is subject to several limitations that merit consideration. Primarily, it is based on a single-center database, and the cohort is predominantly from the Korean population. Consequently, the applicability of our findings to other ethnic or demographic groups may be limited. Moreover, the reliance on data extracted from the INSPIRE database introduces the possibility of compromised data integrity, which could be attributed to incomplete medical records, data entry inaccuracies, or instances of omitted information. These factors collectively could impact the robustness of our conclusions. In light of these limitations, it is imperative that future studies, especially larger-scale randomized controlled trials (RCTs), are undertaken to corroborate and extend our findings across more diverse and representative populations.

Conclusions

The MELD score demonstrates a robust predictive value

for clinical outcomes following cardiac valve surgery, underscoring its utility as a viable metric for disease stratification research. This score, by quantifying the severity of organ dysfunction, provides a reliable gauge for prognostic assessments in the postoperative phase of cardiac interventions.

Acknowledgments

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-242/rc

Peer Review File: Available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-242/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-242/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). Approval for this study was obtained from the Committee on Ethics of Biomedical Research at Shanghai East Hospital, Tongji University School of Medicine, Shanghai (No. TJUSM2023-010), with a waiver for individual patient consent.

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