Association Between Different Versions of the Model for End-Stage Liver Disease Score and Contrast-Associated Acute Kidney Injury in Patients Undergoing Elective Percutaneous Coronary Intervention

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Background: Pre-procedure liver dysfunction was associated with acute kidney injury after percutaneous coronary intervention (PCI). The aim of this study is to assess and compare the predictive value of different liver function scoring systems for contrast-associated acute kidney injury (CA-AKI) in patients undergoing elective PCI.

Methods and Results: A total of 5,569 patients were retrospectively enrolled. The model for end-stage liver disease (MELD) including albumin (MELD-Albumin) score (AUC=0.661) had the strongest predictive value in comparison to the MELD score (AUC=0.627), the MELD excluding the international normalized ratio (MELD-XI) score (AUC=0.560), and the MELD including sodium (MELD-Na) score (AUC=0.652). In the fully adjusted logistic regression model, the MELD-Albumin score and the MELD-Na score were independently associated with CA-AKI regardless of whether they were treated as continuous or categorical variables; however, this was not the case for the MELD score and the MELD-XI score. Furthermore, the addition of the MELD-Albumin score significantly improved the reclassification beyond the fully adjusted logistic regression model. The study further explored the association between different versions of the MELD score and CA-AKI using restricted cubic splines and found a linear relationship between the MELD-Albumin score and the risk of CA-AKI.

Conclusions: The MELD-Albumin score had the highest predictive value for CA-AKI in patients undergoing elective PCI. The addition of the MELD-Albumin score to the existing risk prediction model significantly improved the reclassification for CA-AKI.

Key Words: Albumin; Contrast-associated acute kidney injury; Model for end-stage liver disease; Percutaneous coronary intervention

Contrast-associated acute kidney injury (CA-AKI) is one of the most common complications after percutaneous coronary intervention (PCI), which refers to acute renal impairment caused by the endovascular application of contrast medium. It is associated with prolonged hospitalization, higher medical costs, persistent kidney impairment, dialysis, and increased mortality.¹⁻³

Therefore, accurate identification of patients at high risk of developing CA-AKI before the procedure is of great significance for improving patient prognosis.

Patients with coronary artery disease complicated with liver dysfunction are often accompanied by an increased prevalence of acute kidney injury (AKI) after PCI.^{4,5} Thus, assessing the liver function and determining risk stratification

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before the procedure is a critical step in optimizing patient management. The model for end-stage liver disease (MELD) score, which is a recognized liver function assessment tool, has been proven to be associated with AKI.^{6,7} Furthermore, numerous studies focused on the modified MELD versions and have demonstrated that the MELD excluding the international normalized ratio (MELD-XI) score and the MELD including sodium (MELD-Na) score was also correlated with AKI.⁸⁻¹⁰ However, the predictive value of the MELD including albumin (MELD-Albumin) score for CA-AKI is still unclear. Moreover, there is a lack of research comparing the predictive ability of the MELD score and its modifications for CA-AKI. Consequently, the purpose of the present study was to investigate and compare the predictive value of the MELD score and its modifications for predicting CA-AKI in patients undergoing elective PCI.

Methods

Study Population

The present study was designed as an observational, retrospective study. All patients who underwent elective PCI between January 2012 and December 2018 at Fujian Provincial Hospital were consecutively included in the study and retrospectively analyzed. The exclusion criteria were listed as follows: (1) patients with end-stage renal disease (estimated glomerular filtration rate [eGFR] <15 mL/min/1.73 m²) or those who required long-term dialysis; (2) patients who had been administrated with contrast agents within 1 week before or 48 h after the procedure; (3) patients who took nephrotoxic drugs within 1 week before or 48 h after the procedure; (4) patients who had missing data on total bilirubin, international normalized ratio (INR), serum sodium, albumin, and pre- or post-procedural serum creatinine (SCr); and (5) patients who died within the first 24 h after hospital admission. Finally, 5,569 participants were included in the analysis. This study was conducted in accordance with the Declaration of Helsinki and ethical approval was obtained from the Fujian Provincial Hospital ethics committee (Ethical approval number: K2019-07-011). All patients provided written informed consent.

Protocol

All demographic, clinical, laboratory, and angiographic data were collected via electronic medical records. Venous blood samples were collected on admission or the second day after admission. The SCr concentration was measured before the procedure and consecutive 2 days after the procedure. All patients received non-ionic, low-osmolality contrast medium (either Iopamiron or Ultravist, both 370 mgI/mL) during PCI procedures, which were conducted by experienced interventional cardiologists. An intravenous infusion of 0.9% saline at a rate of 1 mL/kg/h for 12 h was performed for all patients throughout the perioperative period (or 0.5 mL/kg/h among heart failure patients). The choice of pharmaceutical therapy was at the discretion of the treating physician, in accordance with appropriate guidelines.

Definitions and Study Endpoint

The study endpoint was the development of CA-AKI, which was defined as an increase in SCr ≥ 0.3 mg/dL or $\geq 50\%$ within 48 h after the administration of contrast media.¹¹ Anemia was defined as a hematocrit <0.39 (male) or <0.36 (female). We calculated the standard MELD score and its

3 modifications (MELD-XI score, MELD-Na score, and MELD-Albumin score) according to the following formulas: (1) MELD = $3.78 \times \ln(\text{total bilirubin, mg/dL}) + 11.2 \times \ln(\text{INR}) + 9.57 \times \ln(\text{SCr, mg/dL}) + 6.43$; (2) MELD-XI = $5.11 \times \ln(\text{total bilirubin, mg/dL}) + 11.76 \times \ln(\text{SCr, mg/dL}) + 9.44$; (3) MELD-Na = MELD - (serum sodium, mmol/L) - $0.025 \times \text{MELD} \times (140 - \text{serum sodium, mmol/L}) + 140$; (4) MELD-Albumin = $3.78 \times \ln(\text{total bilirubin, mg/dL}) + 11.2 \times \ln[1 + (4.1 - \text{Albumin, g/dL})] + 9.57 \times \ln(\text{SCr, mg/dL}) + 6.43$ (if the value of albumin was <4.1 g/dL) or MELD-Albumin = $3.78 \times \ln(\text{total bilirubin, mg/dL}) + 11.2 \times \ln(1) + 9.57 \times \ln(\text{SCr, mg/dL}) + 6.43$ (if the value of albumin was >4.1 g/dL).¹²⁻¹⁴ To avoid a negative score, the lower limit of all parameters was set at 1.0. The serum sodium values ≤ 125 mmol/L will be set to 125 mmol/L, and values ≥ 140 mmol/L will be set to 140 mmol/L. The eGFR was calculated using the modified Modification of Diet in Renal Disease equation: $\text{eGFR} = 186.3 \times (\text{SCr})^{-1.154} \times (\text{age})^{-0.203} \times 0.742$ (if the patient was female).¹⁵

Statistical Analysis

Statistical analyses were conducted using the R statistical language (R Foundation for Statistical Computing, Vienna, Austria; version 4.0.2). Continuous variables were presented in the form of mean $\pm$ standard deviation (SD) or median (interquartile range) and analyzed using the Student's t-test (normally distributed) or Mann-Whitney U-test (non-normally distributed). Categorical variables were summarized as counts (percentage) and compared using the chi-squared test or Fisher's exact test.

The association between different versions of the MELD score and CA-AKI was evaluated by logistic analysis using 3 multivariate models. The significant variables determined by univariate logistic analysis based on a significance threshold of P value <0.05 and those of clinical importance were incorporated into multivariate analysis. Model 1 was adjusted for age >75 years and gender. Model 2 included variables from Model 1 plus diabetes, hypertension, history of myocardial infarction (MI), anemia, left ventricular ejection fraction (LVEF) <40%, chronic kidney disease (CKD), hyperuricemia, acute MI, contrast volume >150 mL, and multivessel disease. Model 3 was further adjusted for variables used in Model 2 and added in white blood cell (WBC), high-density lipoprotein-cholesterol (HDL-C), and glucose. For the subgroup analyses, the presence of interaction was determined across various subgroups. To further explore the potential linear and non-linear associations between different versions of the MELD score and the odds ratio (OR) of CA-AKI after adjusting for confounding factors, as Model 3 used in the logistic analysis, restricted cubic splines with 3 knots were used.

According to the receiver operating characteristic curve (ROC) analysis, the optimal cut-off values of the MELD score and its modifications for predicting CA-AKI were determined by maximizing the Youden index. The area under the curve (AUC), continuous net reclassification improvement (NRI), and integrated discrimination improvement (IDI) values were used to compare the predictive power of the MELD score and its modifications on CA-AKI. Differences in AUCs were compared using the DeLong method. In addition, we calculated the C-statistics, continuous NRI, and IDI to examine the incremental effects of the MELD score and its 3 modifications on the predictive potential of Model 3. Two-sided P < 0.05 was considered statistically significant.

Table 1. Baseline Characteristics of the Study Population

Variables	Total (n=5,569)	Non-CA-AKI (n=5,218)	CA-AKI (n=351)	P value
Demographics				
Age, years	65.4±10.5	65.1±10.4	68.6±11.2	<0.001
Age >75 years, n (%)	989 (17.8)	884 (16.9)	105 (29.9)	<0.001
Sex, female, n (%)	1,194 (21.4)	1,089 (20.9)	105 (29.9)	<0.001
BMI, kg/m ²	24.45±3.24	24.47±3.24	24.12±3.34	0.077
Medical history, n (%)				
History of MI	734 (13.2)	692 (13.3)	42 (12.0)	0.540
Diabetes	1,977 (35.5)	1,823 (34.9)	154 (43.9)	0.001
Hypertension	3,782 (67.9)	3,515 (67.4)	267 (76.1)	0.001
Acute MI	1,757 (31.5)	1,552 (29.7)	205 (58.4)	<0.001
Anemia	1,525 (27.4)	1,370 (26.3)	155 (44.2)	<0.001
CKD	548 (9.8)	479 (9.2)	69 (19.7)	<0.001
Hyperuricemia	1,709 (30.7)	1,578 (30.2)	131 (37.3)	0.006
Procedure performed				
Multivessel disease, n (%)	4,473 (83.3)	4,178 (83.0)	295 (87.8)	0.027
Number of stents	1.64±0.88	1.64±0.87	1.67±0.97	0.595
Stent length, mm	44.62±26.92	44.53±26.80	45.88±28.62	0.372
Contrast volume >150 mL, n (%)	3,860 (72.4)	3,617 (72.3)	243 (73.6)	0.647
Medical therapy during hospitalization, n (%)				
Antiplatelet	5,556 (99.8)	5,207 (99.8)	349 (99.4)	0.437
Statin	5,519 (99.1)	5,172 (99.1)	347 (98.9)	0.839
ACEI/ARB	4,602 (82.6)	4,300 (82.4)	302 (86.0)	0.096
β-blocker	4,602 (82.6)	4,299 (82.4)	303 (86.3)	0.070
CCB	1,965 (35.3)	1,830 (35.1)	135 (38.5)	0.219
Warfarin	79 (1.5)	68 (1.4)	11 (3.5)	0.006
Laboratory measurements				
Serum creatinine, mg/dL	0.92±0.28	0.92±0.27	0.94±0.38	0.136
eGFR, mL/min/1.73m ²	89.64±24.21	89.55±23.17	90.98±36.36	0.285
WBC, 10 ⁹ /L	7.38±2.33	7.33±2.28	7.99±2.87	<0.001
Platelet, 10 ⁹ /L	222.56±68.71	222.72±69.04	220.28±63.57	0.521
Albumin, g/dL	4.13±0.41	4.15±0.40	3.89±0.46	<0.001
Total bilirubin, mmol/L	0.60 (0.44–0.82)	0.60 (0.44–0.81)	0.58 (0.45–0.88)	0.526
ALT, U/L	23.00 (16.00–35.00)	23.00 (16.00–35.00)	23.00 (15.00–37.00)	0.865
AST, U/L	22.00 (17.00–31.00)	21.00 (17.00–30.00)	25.00 (18.00–51.00)	<0.001
ALP, U/L	72.00 (60.00–88.00)	72.00 (60.00–88.00)	73.00 (61.75–88.50)	0.304
GGT, U/L	32.00 (21.00–50.00)	32.00 (21.00–50.00)	34.00 (21.00–54.25)	0.449
Cholesterol, mg/dL	163.57±44.86	163.19±44.86	165.12±43.70	0.459
Triglyceride, mmol/L	122.19 (91.20–172.66)	122.19 (91.20–173.55)	122.19 (90.32–165.58)	0.676
HDL-C, mg/dL	40.22±11.21	40.22±11.21	38.67±10.05	0.019
LDL-C, mg/dL	105.18±39.06	104.80±39.06	107.12±38.67	0.319
Glucose, mg/dL	110.16±36.18	109.44±35.46	118.98±45.90	<0.001
INR	1.03±0.17	1.02±0.17	1.06±0.20	<0.001
Serum sodium, mmol/L	140.15±3.58	140.23±3.51	138.85±4.34	<0.001
MELD score	6.88 (6.43–7.90)	6.87 (6.43–7.83)	7.60 (6.65–8.96)	<0.001
MELD-XI score	9.44 (9.44–10.28)	9.44 (9.44–10.21)	9.44 (9.44–11.47)	<0.001
MELD-Na score	7.61 (6.60–9.58)	7.57 (6.54–9.40)	9.09 (7.37–11.82)	<0.001
MELD-Albumin score	7.39 (6.43–9.59)	7.28 (6.43–9.37)	9.11 (7.02–12.17)	<0.001
LVEF <40%, n (%)	155 (2.9)	128 (2.6)	27 (8.0)	<0.001

ACEI/ARB, angiotensin-converting enzyme inhibitor/angiotensin receptor blocker; ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; CA-AKI, contrast-associated acute kidney injury; CCB, calcium channel blockers; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; GGT, gamma-glutamyl transpeptidase; HDL-C, high-density lipoprotein-cholesterol; INR, international normalized ratio; LDL-C, low-density lipoprotein-cholesterol; LVEF, left ventricular ejection fraction; MI, myocardial infarction; MELD, model for end-stage liver disease; MELD-Albumin, model for end-stage liver disease including albumin; MELD-Na, model for end-stage liver disease including sodium; MELD-XI, model for end-stage liver disease excluding the international normalized ratio; WBC, white blood cell.

Figure 1. Receiver operating characteristic curve analysis of the MELD score and its modifications for predicting CA-AKI. CA-AKI, contrast-associated acute kidney injury; MELD, model for end-stage liver disease; MELD-Albumin, model for end-stage liver disease including albumin; MELD-Na, model for end-stage liver disease including sodium; MELD-XI, model for end-stage liver disease excluding the international normalized ratio.

Table 2. Comparison of the Predictive Value of the MELD Score and Its Modifications for CA-AKI

	AUC	P value	Continuous NRI (95% CI)	P value	IDI (95% CI)	P value
MELD-Albumin vs. MELD	0.661 vs. 0.627	0.022	0.448 (0.340–0.555)	<0.001	0.018 (0.013–0.023)	<0.001
MELD-Albumin vs. MELD-XI	0.661 vs. 0.560	<0.001	0.485 (0.377–0.592)	<0.001	0.020 (0.015–0.024)	<0.001
MELD-Albumin vs. MELD-Na	0.661 vs. 0.652	0.556	0.308 (0.200–0.415)	<0.001	0.010 (0.004–0.016)	<0.001

AUC, area under the curve; CI, confidence interval; IDI, integrated discrimination improvement; NRI, net reclassification improvement. Other abbreviations as in Table 1.

Results

Patients Characteristics

Among the 5,569 patients enrolled, 351 (6.3%) patients developed CA-AKI. The mean age of our study population was 65.4 ± 10.5 years and 989 (17.8%) patients were aged >75 years. Most patients were men (78.6%) and 734 (13.2%) had a history of MI. Patients who developed CA-AKI were more likely to have acute MI, anemia, CKD, hyperuricemia, multivessel disease, and a history of diabetes and hypertension. They also had higher levels of WBC and glucose, but lower levels of albumin, HDL-C, serum sodium, and LVEF. The MELD score, MELD-XI score, MELD-Na score, and MELD-Albumin score were higher in patients with CA-AKI than those without CA-AKI. More information on the baseline characteristics is detailed in Table 1.

Predictive Value of the MELD Score and Its 3 Modifications on CA-AKI

According to the ROC analysis, the optimal cut-off value of the MELD score, MELD-XI score, MELD-Na score,

and MELD-Albumin score for predicting CA-AKI were 7.6, 11.2, 8.2, and 7.9, respectively. The MELD-Albumin score had higher AUC values than the MELD score (0.661 vs. 0.627, $P=0.022$) and the MELD-XI score (0.661 vs. 0.560, $P<0.001$), but similar AUC values to the MELD-Na score (0.661 vs. 0.652, $P=0.556$) (Figure 1). Further NRI and IDI analysis indicated that the MELD-Albumin score significantly improved the reclassification and discrimination ability for the prediction of CA-AKI beyond the MELD score, MELD-XI score, and MELD-Na score (all $P<0.001$) (Table 2).

Effect of the MELD Score and Its 3 Modifications on CA-AKI

The association between different versions of the MELD score and CA-AKI was investigated by using univariate and multivariate logistic regression models. When different versions of the MELD score were analyzed as binary variables according to their optimal cut-off values, the MELD score and its 3 modifications were independently associated with CA-AKI, regardless of which model was used for adjustment. When analyzed as continuous variables, only the MELD-Na score (OR=1.065; 95% CI, 1.024–1.109 per

Table 3. Univariate and Multivariate Logistic Regression Analyses of the Association Between Different Versions of the MELD Score and CA-AKI

	Unadjusted		Model 1		Model 2		Model 3	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
MELD, continuous								
Per 1-point increment	1.141 (1.095–1.189)	<0.001	1.129 (1.082–1.179)	<0.001	1.050 (0.987–1.118)	0.125	1.039 (0.975–1.107)	0.234
MELD, categorical								
MELD ≤7.6	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
MELD >7.6	2.376 (1.911–2.953)	<0.001	2.373 (1.894–2.972)	<0.001	1.723 (1.316–2.257)	<0.001	1.643 (1.250–2.159)	<0.001
MELD-XI, continuous								
Per 1-point increment	1.131 (1.081–1.183)	<0.001	1.124 (1.073–1.177)	<0.001	1.016 (0.941–1.097)	0.683	1.005 (0.930–1.086)	0.893
MELD-XI, categorical								
MELD-XI ≤11.2	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
MELD-XI >11.2	2.150 (1.684–2.746)	<0.001	2.155 (1.673–2.777)	<0.001	1.600 (1.123–2.281)	0.009	1.492 (1.043–2.134)	0.029
MELD-Na, continuous								
Per 1-point increment	1.145 (1.112–1.179)	<0.001	1.138 (1.104–1.173)	<0.001	1.077 (1.036–1.120)	<0.001	1.065 (1.024–1.109)	0.002
MELD-Na, categorical								
MELD-Na ≤8.2	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
MELD-Na >8.2	2.479 (1.985–3.095)	<0.001	2.468 (1.963–3.102)	<0.001	1.721 (1.327–2.232)	<0.001	1.617 (1.240–2.109)	<0.001
MELD-Albumin, continuous								
Per 1-point increment	1.193 (1.157–1.231)	<0.001	1.184 (1.147–1.223)	<0.001	1.105 (1.057–1.156)	<0.001	1.097 (1.047–1.148)	<0.001
MELD-Albumin, categorical								
MELD-Albumin ≤7.9	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
MELD-Albumin >7.9	2.900 (2.310–3.640)	<0.001	2.751 (2.180–3.470)	<0.001	1.712 (1.300–2.254)	<0.001	1.651 (1.250–2.180)	<0.001

Model 1: Adjusted for age >75 years and gender. Model 2: Adjusted for variables from Model 1 plus diabetes, hypertension, history of MI, anemia, LVEF <40%, CKD, hyperuricemia, acute MI, contrast volume >150 mL, and multivessel disease. Model 3: Adjusted for variables from Model 2 plus WBC, HDL-C, and glucose. OR, odds ratio. Other abbreviations as in Tables 1,2.

1-point increment; $P=0.002$) and MELD-Albumin score ($OR=1.097$; 95% CI, 1.047–1.148 per 1-point increment; $P<0.001$) were independent risk factors for CA-AKI after adjusting for model 3; however, this was not the case for the MELD score ($OR=1.039$; 95% CI, 0.975–1.107 per 1-point increment; $P=0.234$) and the MELD-XI score ($OR=1.005$; 95% CI, 0.930–1.086 per 1-point increment; $P=0.893$) (Table 3). In most subgroups, no significant interaction effect between different versions of the MELD score and CA-AKI was found (Figure 2 and Supplementary Figures 1–3). We further evaluated the relationship between different versions of the MELD score and the OR of CA-AKI after adjusting for confounding factors that Model 3 used in logistic analysis using restricted cubic splines with 95% confidence intervals. A linear relationship between the MELD-Albumin score and the risk of CA-AKI was found (Figure 3A–D).

Incremental Effects of MELD Score and Its 3 Modifications on the Predictive Potential of Model 3 for CA-AKI

The addition of the MELD score and its 3 modifications did not have significant incremental effects on the AUC of model 3 (all P for comparison >0.05); however, the addition of the MELD-Albumin score significantly improved

the reclassification and discrimination ability beyond model 3, with a continuous NRI of 0.438 and an IDI of 0.006 (both $P<0.001$) (Table 4).

Discussion

In this retrospective study, we discovered that the MELD-Albumin score had the highest predictive value for predicting CA-AKI than other versions of the MELD score in patients undergoing elective PCI. There is a linear relationship between the MELD-Albumin score and the risk of CA-AKI. Furthermore, the addition of the MELD-Albumin score significantly improved the reclassification and discrimination ability beyond the fully adjusted logistic regression model.

Patients with liver dysfunction treated with PCI were more susceptible to developing AKI and this was closely related to poor prognosis. In a large, patient-level study using the national inpatient sample, an all-payer claims database in the United States, patients with cirrhosis who underwent PCI had a higher risk of AKI and in-hospital mortality than those without cirrhosis.⁴ Another large study also detected a higher rate of AKI, gastrointestinal bleeding, and 90-day mortality in patients with cirrhosis

MELD-Albumin score and CA-AKI

Figure 2. Forrest plots of subgroup analysis of the association between the MELD-Albumin score and CA-AKI. CA-AKI, contrast-associated acute kidney injury; MELD-Albumin, model for end-stage liver disease including albumin.

Figure 3. Restricted cubic spline curves with logistic regression between different versions of the MELD score and CA-AKI. Black dashed horizontal lines represent the odds ratio of 1.0. Red lines indicate the estimated odds ratio (OR), and the shaded ribbons represent a 95% confidence interval (CI). OR (95% CI) were all adjusted according to Model 3 in logistic analysis. (A) Association between the MELD score and CA-AKI. (B) Association between the MELD-XI score and CA-AKI. (C) Association between the MELD-Na score and CA-AKI. (D) Association between the MELD-Albumin score and CA-AKI. CA-AKI, contrast-associated acute kidney injury; MELD, model for end-stage liver disease; MELD-Albumin, model for end-stage liver disease including albumin; MELD-Na, model for end-stage liver disease including sodium; MELD-XI, model for end-stage liver disease excluding the international normalized ratio.

Table 4. Model Performance After the Addition of the MELD Score or Its Modifications to Model 3 for Predicting CA-AKI

Model	C-statistic	P value	Continuous NRI	P value	IDI	P value
Model 3*	0.739	Ref.	Ref.		Ref.	
Model 3+MELD (categorical)	0.745	0.117	0.314	<0.001	0.004	0.069
Model 3+MELD-XI (categorical)	0.741	0.344	0.276	<0.001	0.001	0.396
Model 3+MELD-Na (categorical)	0.745	0.116	0.354	<0.001	0.003	0.108
Model 3+MELD-Albumin (categorical)	0.742	0.414	0.438	<0.001	0.006	<0.001

*Model 3 includes the following parameters: age >75 years, gender, diabetes, hypertension, history of MI, anemia, LVEF <40%, CKD, hyperuricemia, acute MI, contrast volume >150 mL, multivessel disease, WBC, HDL-C, and glucose. Abbreviations as in Tables 1,2.

receiving PCI than those without cirrhosis.⁵ Consequently, assessing the liver function before the procedure has significant clinical value for optimizing patient management and improving patient prognosis.

As early as 2000, Malinchoc et al established the MELD score based on 3 commonly used clinical parameters. The MELD score was originally developed as a valuable tool for assessing liver function and had been demonstrated to

be associated with poor short-term prognosis in patients with cirrhosis who received a transjugular intrahepatic portosystemic shunt.¹⁶ Recently, many studies extended the application scope of the MELD score and determined the association between the MELD score and adverse outcomes in patients who underwent PCI.^{17,18} Furthermore, numerous studies have focused on the predictive value of the MELD score and its modifications on AKI. A multi-

center prospective cohort study of patients with severe alcoholic hepatitis conducted by Sujan et al discovered that a higher MELD score at admission can predict inpatient AKI.⁶ Tariq et al performed a meta-analysis involving 18,474 patients with cirrhosis and found that the MELD score was related to AKI.⁷ In addition, an increased MELD-XI score was validated to be an independent risk factor for AKI in patients with postcardiotomy cardiogenic shock treated with venoarterial extracorporeal membrane oxygenation by another retrospective study.⁸ Similarly, in a prospective observational study, 131 patients who underwent hepatobiliary surgeries were analyzed and it was suggested that a higher level of the MELD-Na score was significantly associated with an increased risk of developing AKI.⁹ Bao et al retrospectively evaluated patients who required orthotopic liver transplantation and identified a correlation between the MELD-Na score and AKI.¹⁰ However, to our knowledge, there are no studies that explored the predictive value of the MELD-Albumin score for CA-AKI. In addition, no study has directly compared the predictive value of the MELD score and its modifications for predicting CA-AKI. Our study assessed and compared the predictive value of different versions of the MELD score and showed that the MELD-Albumin score had the highest predictive value for predicting CA-AKI than the MELD score, the MELD-XI score, and the MELD-Na score in patients undergoing elective PCI. The addition, the MELD-Albumin score significantly improved the reclassification and discrimination ability beyond the fully adjusted logistic regression model, with a continuous NRI of 0.438 and an IDI of 0.006 (both $P < 0.001$). Moreover, the odds of developing CA-AKI increased almost linearly with an increasing value of the MELD-Albumin score.

Actually, previous studies have demonstrated that the components of the MELD-Albumin score (total bilirubin, albumin, and SCr) were associated with CA-AKI. Bilirubin is a physiologic antioxidant and free radical scavenger,¹⁹ which can protect renal function when the total bilirubin was mildly elevated within the normal range (laboratory normal range in our study was 0.1–1.0 mg/dL).²⁰ However, Wu et al discovered that a higher level of total bilirubin was associated with an increased incidence of CA-AKI when the concentration of total bilirubin exceeded the normal range.²⁰ It indicates that severe hyperbilirubinemia may induce the development of CA-AKI via reducing renal perfusion by decreasing the arterial pressure and intraglomerular pressure.²¹ In the formula of the MELD-Albumin score, the lower limit of total bilirubin was set at 1.0 mg/dL, which is the upper limit of the normal range in our study; therefore, the value of the MELD-Albumin score elevated with increasing total bilirubin levels. Albumin, as a protein produced by the liver, is an important and recognized indicator of the synthetic function of the liver.²² The level of serum albumin reduces when the synthetic function of the liver decreases. Serum albumin has several functions including maintaining colloid osmotic pressure and increasing renal perfusion.^{23,24} Additionally, serum albumin also acts as an antioxidant by scavenging free radicals,²⁵ which can reduce the risk of CA-AKI. Several studies have also detected a relationship between lower levels of serum albumin and CA-AKI.^{26–28} The MELD-Albumin score increased as the level of albumin decreased. SCr is used for the evaluation of renal function. Poor renal function has been shown to increase the risk of CA-AKI.²⁹

In summary, the MELD-Albumin score combines these 3 parameters and can simultaneously evaluate liver and renal function. Our data showed that patients who developed CA-AKI have a higher level of aspartate aminotransferase (AST) and INR, and a lower level of serum albumin than patients who did not develop CA-AKI. Additionally, patients who developed CA-AKI have a higher incidence of CKD compared with those who did not develop CA-AKI. Taken together, we consider that patients who developed CA-AKI may have a worse liver and renal function than those who did not develop CA-AKI. Besides, in the high MELD-Albumin score group (MELD-Albumin score >7.9), the level of AST, and INR was higher and the level of serum albumin was lower as compared to the low MELD-Albumin score group (MELD-Albumin score ≤ 7.9). The incidence of CKD was also higher in the high MELD-Albumin score group (MELD-Albumin score >7.9) than in the low MELD-Albumin score group (MELD-Albumin score ≤ 7.9) (**Supplementary Table**). It indicates that patients with a higher MELD-Albumin score are more likely to have a worse liver and renal function, which is associated with CA-AKI.

Apart from the mechanisms mentioned above, some factors that lead to liver injuries such as autoimmune disease, various drugs and toxins, and hepatitis C virus, may trigger systemic inflammation and oxidative stress.^{30,31} This may ultimately result in CA-AKI because inflammation and oxidative stress are important pathophysiological mechanisms of CA-AKI.³² Additionally, the balance of vasoconstrictors and vasodilators is disrupted in the context of liver dysfunction, which causes splanchnic and systemic vasodilation and renal vasoconstriction. These conditions eventually lead to the impairment of renal function.³³ Therefore, the correction of liver function before the procedure has important clinical implications for improving patient outcomes.

As we mentioned above, the MELD score was originally developed to predict short-term poor prognosis of patients with cirrhosis who received a transjugular intrahepatic portosystemic shunt.¹⁶ Recently, a growing number of studies have demonstrated that the MELD-based scoring system could be used as a marker of cardiovascular risk in patients undergoing PCI, even in patients without end-stage liver disease.^{17,18,34} Individual components of the MELD-Albumin score (total bilirubin, albumin, and SCr) have been previously demonstrated to be associated with CA-AKI.^{26,27,29,35} Furthermore, our study also discovered that the MELD-Albumin score was strongly associated with CA-AKI in patients undergoing elective PCI. Collectively, these data indicated that a cluster of risk factors included in the MELD-Albumin score might also provide potential predictive information on CA-AKI in the general population, including those without cirrhosis.

Several limitations exist in this study that need to be mentioned. First, the risk of selection bias cannot be ruled out due to the retrospective nature of our study. Second, we only calculated the MELD score and its modifications at a single time because the critical laboratory parameters included in the formula were measured only once. Therefore, random errors were inevitably introduced in the present study. Third, we did not include the etiology of liver dysfunction as a parameter in the analysis. The lack of relevant data limits the assessment of these variables. Fourth, as we mentioned above, autoimmune disease, various drugs and toxins, and hepatitis C virus may trigger systemic inflam-

mation and oxidative stress. This may increase the risk of developing CA-AKI because inflammation and oxidative stress are important pathophysiological mechanisms of CA-AKI. However, we did not collect information about autoimmune disease, hepatitis C virus, and parameters reflecting inflammation and oxidative stress such as C-reactive protein, procalcitonin, and interleukin-6. Therefore, the mechanistic explanation for the association between the MELD-Albumin score and CA-AKI is speculative. Future studies are needed to further explore the specific mechanisms. Fifth, the long-term use of oral anticoagulants before admission may affect the measurement of INR, which could confound the results. However, we performed a sensitivity analysis by excluding patients who were taking warfarin from the main analysis and found that our main conclusions were not affected by these differences (data not shown). Finally, despite several confounding factors being adjusted for, the results of our study may have been subjected to residual confounding factors.

In conclusion, the MELD-Albumin score had the highest predictive value for predicting CA-AKI than other versions of the MELD score in patients undergoing elective PCI. There is a linear relationship between the MELD-Albumin score and the risk of CA-AKI. The addition of the MELD-Albumin score to the existing risk prediction model significantly improved the reclassification and discrimination ability for CA-AKI.

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Disclosures

The authors declare that there are no conflicts of interest.

IRB Information

This study was approved by the ethics committee of Fujian Provincial Hospital (Ethical approval number: K2019-07-011).

Data Availability

The deidentified participant data will not be shared.

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Supplementary Files

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