Original Article

Model for End-stage Liver Disease Excluding International Normalized Ratio (MELD-XI) Score Independently Predicts In-Hospital Cardiac and 1-Year All-Cause Mortality in Noncardiac Surgery

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Abstract

Objective: Cardiac adverse events are one of the most-feared complications among patients undergoing noncardiac surgery. Model for end-stage liver disease excluding international normalized ratio (MELD-XI) score has been shown to carry prognostic implications for patients with various cardiac conditions, but it has not been used for patients undergoing noncardiac surgery. We aimed to determine the role of MELD-XI score for the prediction of mortality in high-risk noncardiac surgical candidates. **Materials and Methods:** Eighty-four patients with high-risk cardiac conditions undergoing elective or urgent noncardiac surgery were reviewed for in-hospital cardiac and 1-year all-cause mortality. MELD-XI score was compared between the surviving and deceased patients. It was correlated with both mortality rates; its predictive power for mortality prediction was tested. **Results:** The median age was 81 (interquartile range 18) years, and 41 (48.8%) patients were male. All patients had at least one high-risk cardiac condition. Forty patients experienced a cardiac adverse event. Sixteen (19%) patients died at hospital and 40 (47.6%) patients died by 1 year, and both groups had significantly higher MELD-XI scores than survivors (12.23 [6.53] vs. 9.66 [3.81]; $P = 0.001$ and 10.80 [6.31] vs. 9.70 [3.70]; $P = 0.037$, respectively). MELD-XI score independently predicted in-hospital cardiac mortality (OR: 1.254 [95% confidence interval [CI]: 1.028–1.530]; $P < 0.05$) and 1-year all-cause mortality (OR: 1.258 [95% CI: 1.057–1.498; $P < 0.01$). MELD-XI predicted in-hospital cardiac mortality with a fair sensitivity and a moderate specificity and 1-year all-cause mortality with a fair sensitivity but poor specificity. A MELD-XI score >8.87 was associated with a significantly worse 1-year survival (log rank test, $P < 0.05$). **Conclusion:** MELD-XI score is independently associated with in-hospital cardiac and 1-year all-cause mortality among high-risk patients undergoing noncardiac surgery.

Keywords: Cardiac, high-risk, Model for end-stage liver disease excluding international normalized ratio score, mortality, noncardiac surgery

Introduction

Cardiac adverse events including death are one of the most feared complications of noncardiac surgery, for which several high-risk cardiac conditions have been defined and a number of risk scores have been developed.[1-3] Model for end-stage

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liver disease (MELD) score was developed to predict clinical outcomes primarily in patients with liver disease,[4,5] but it has also been used in patients with multiorgan failure,[6] heart failure,[7] or left ventricular assist devices (LVADs).[8-10] MELD-XI score is a derivative of MELD score, calculated by excluding international normalized ratio (INR) from the parameters for patients who use anticoagulants. MELD-XI score has also been shown to predict mortality in various cardiac conditions.[11-16] Herein, we aimed to study MELD-XI score to predict mortality among high-risk patients undergoing elective or urgent noncardiac surgery.

Materials and Methods

This study was approved by the Local Ethics Committee (Approval Date 25.04.2019, Approval No.: KA 19/156) and supported by the Local University Research Fund. The demographic, clinical, electrocardiographic, echocardiographic, and biochemical data of 84 patients who underwent elective or urgent noncardiac surgery under general anesthesia between January 1, 2013, and January 1, 2018, were retrospectively reviewed from written medical records and hospital data automation system.

The type of elective or urgent noncardiac surgery and risk status of the individual patients were recorded, and only high-risk noncardiac surgical candidates were enrolled.[1] The elective noncardiac surgical operations included in the present the study were the ones that could not be delayed due to the severity of the underlying condition, where the risk of postponing surgery would outweigh surgical risk. The risk of noncardiac surgery was determined by the consulting cardiologist. The high-risk cardiac conditions included all vascular diseases undergoing surgery; severe aortic stenosis, as defined as a mean transaortic gradient ≥40 mmHg and/or a valve area <1.0 cm^2 on transthoracic echocardiography; severe mitral stenosis, as defined as a mean transmitral gradient of ≥10 mmHg and/or a mitral valve area <1 cm^2 on transthoracic echocardiography; severe pulmonary arterial hypertension defined as a mean pulmonary artery pressure of ≥70 mmHg on transthoracic echocardiography and/or a mean pulmonary artery pressure of ≥40 on a recent cardiac catheterization; multiple prosthetic heart valves; serious ventricular arrhythmias including ventricular tachycardia, ventricular flutter, or ventricular fibrillation, or frequent ventricular premature depolarizations with reduced left ventricular systolic function; atrial fibrillation or flutter with rapid ventricular rate response (>110/min at rest); recent or current acute coronary syndromes or myocardial infarction; severe decompensated or low-output heart failure; and uncontrollable angina pectoris despite maximal medical therapy or previous coronary intervention. None of the patients underwent surgical or percutaneous correction of high-risk cardiac conditions due to either urgency of noncardiac surgery or presence of multiple comorbidity risking procedural safety, such as hematological disorders (coagulopathies, bleeding diatheses, and anticoagulant use), acute renal failure, acute hepatic failure, contrast agent allergy, active infection, hypoxemia or decompensated heart failure, or overall poor patient status. All patients received appropriate therapy against individual high-risk cardiac conditions, including anti-ischemic therapy composed of oxygen, beta-blockers, nitrates, acetylsalicylic acid, and statins; appropriate antihypertensive therapy using intravenous or oral antihypertensives for uncontrolled or severe hypertension; heart rate control using digoxin, beta-blockers or non-dihydropyridine calcium channel blockers, and anticoagulation with low-molecular-weight heparin for atrial fibrillation or atrial flutter; prompt defibrillation or cardioversion plus amiodarone and electrolyte replacement for serious ventricular arrhythmias; loop diuretics, aldosterone antagonists, oxygen, nitrates, beta-blockers and angiotensin-converting enzyme inhibitors or angiotensin receptor blockers for decompensated heart failure; and diuretics, beta-blockers, and/or calcium channel blockers for severe mitral stenosis.

Preoperative revised cardiac risk index (Lee score), which was developed for perioperative cardiac adverse events in 1999,[3] was calculated for all patients using six risk factors including high-risk type of surgery (intraperitoneal, intrathoracic, or suprainguinal vascular), history of coronary artery disease (IHD), history of congestive heart failure, history of cerebrovascular disease, preoperative insulin treatment, and preoperative serum creatinine >2.0 mg/dL. MELD-XI score was calculated using the logarithmic conversions of serum creatinine and total serum bilirubin in the following manner: 5.11× ln (serum bilirubin in mg/dL) + 11.76 × ln (serum creatinine in mg/dL) +9.44. Serum creatinine and total bilirubin values below 1.0 mg/dL were rounded up to 1 mg/dL. Serum creatinine values of patients receiving hemodialysis were set to 4 mg/dL.

All in-hospital perioperative cardiac adverse events and deaths were recorded. Cardiac adverse events were defined as perioperative ischemia and/or infarction, pulmonary thromboembolism, ventricular tachycardia, fibrillation, asystole, high-grade atrioventricular block, supraventricular tachycardia with rapid ventricular response, and decompensated and/or low-output heart failure. Cardiac death was defined as that occurring due to the following: myocardial infarction and/or ischemia as evidenced by typical ischemic ECG changes and/or typical rise and fall of cardiac biomarkers of injury; serious ventricular tachyarrhythmias, serious bradyarrhythmias and asystole, supraventricular arrhythmias with rapid ventricular rate response, pericardial tamponade, acute aortic dissection, coronary dissection or embolism, and pulmonary thromboembolism. Information about postdischarge 1-year all-cause mortality was obtained from the records of the local births, deaths, and marriages registration office.

The exclusion criteria were as follows: undergoing cardiac or low-to-intermediate risk surgery; surgical or transcatheter correction of cardiac high-risk condition before noncardiac surgery, thus reducing perioperative risk; postdischarge deaths due to suicide, homicide, accidents, or intoxications; and unknown postdischarge survival status.

No patient consent was obtained from any patient due to the retrospective nature of the study.

Statistical analysis

The study data were analyzed using SPSS (Statistical Package for the Social Sciences) Windows 21.0 (IBM Inc, USA) software. The distribution of continuous variables was tested using the Kolmogorov–Smirnov test. The normally distributed continuous variables were expressed as mean ± standard deviation; the nonnormally distributed ones as median and interquartile range (IQR); and categorical variables as number and percentage. Normally distributed continuous variables were compared with the independent samples *t*-test; nonnormally distributed continuous variables with the Mann–Whitney-U-test; and the categorical variables with the Chi-square test.

The significant predictors of both in-hospital total and 1-year mortality were initially tested with a univariate analysis using all available demographic, clinical, biochemical, and echocardiographic variables. All univariate predictors of mortality with $P < 0.25$ were then used in a binary logistic regression model with backward LR method to determine the independent predictors of both mortality rates. Receiver operating characteristic (ROC) curve was drawn to determine a significant cutoff point of MELD-XI score for in-hospital cardiac and 1-year all-cause mortality. Log-rank test and Kaplan–Meier survival analysis were performed to assess the effect of MELD-XI score on 1-year all-cause survival. $P < 0.05$ was considered statistically significant for all tests.

Results

The overall characteristics of the study population are shown in Table 1. All patients underwent elective or urgent noncardiac surgery under general anesthesia, and the majority (71.4%) of patients underwent general surgery or orthopedic operations. A total of 60 (71.4%) operations were urgent; 24 (28.6%) operations were elective. The most common cardiac high-risk conditions were decompensated heart failure, atrial fibrillation/flutter with rapid ventricular response (each 21.8%), severe valvular stenosis (17.2%), and pulmonary hypertension (16.1%). Forty (47.6%) patients experienced perioperative adverse cardiac events [Table 2]. A total of 16 (19.0%) patients died during perioperative period and 24 (28.6%) patients died by 1 year after hospital discharge, so that a total of 40 (47.6%) patients died by 1 year. The documented cardiac adverse events and etiologies of in-hospital cardiac death are shown in Table 2. Those who died at hospital had a significantly higher serum creatinine level ($P < 0.01$), hemoglobin level ($P < 0.05$), and rate of angina pectoris ($P < 0.05$), but a lower rate of perioperative beta-blocker use ($P < 0.05$) compared to the survivors. Patients who died by the end of 1 year had a significantly lower hemoglobin level, a significantly higher serum AST level, and a significantly higher rate of pulmonary hypertension ($P < 0.05$ for all comparisons) than the survivors. Other clinical, demographic, and laboratory data were similar between the deceased and surviving patients [Tables 3 and 4].

The comparison of revised cardiac risk index (Lee) score between the deceased and survivor groups revealed that it was significantly higher in the patients with in-hospital mortality, but not in those that died by 1 year (3 [3] vs. 2 [1]; $P < 0.05$ and 2 [2] vs. 1.5 [1]; $P = 0.141$, respectively). MELD-XI score, on the other hand, was significantly higher in patients with both in-hospital and long-term mortality (12.23 [IQR: 6.53] vs. 9.66 [IQR: 3.81]; $P = 0.001$ and 10.80 [IQR: 6.31] vs. 9.70 [IQR: 3.70]; $P = 0.037$, respectively) [Tables 3 and 4, respectively]. In univariate analysis, in-hospital cardiac mortality was significantly correlated with MELD-XI score, revised cardiac risk index (Lee) score, cardiac adverse events, serum creatinine level, and serum hemoglobin count ($P < 0.05$ for all), while 1-year all-cause mortality was significantly correlated with MELD-XI score and hemoglobin count ($P < 0.05$ for both comparisons), but not to revised cardiac risk index (Lee) score. A multivariate analysis showed that MELD-XI score independently predicted in-hospital all-cause mortality (OR: 1.254 [95% confidence interval (CI): 1.028–1.530]; $P < 0.05$) and 1-year mortality (OR: 1.258 [95% CI: 1.057–1.498]; $P < 0.01$). In ROC analysis, a MELD-XI score of >10.70 significantly predicted in-hospital cardiac mortality with a sensitivity of 75.0% and a specificity of 63.2% (AUC: 0.760; 95% CI: 0.640–0.880; $P = 0.01$) [Figure 1]; a MELD-XI score of >9.87 was associated with 1-year all-cause mortality with a sensitivity of 80% and a specificity of 40.9% (AUC: 0.633; 95% CI: 0.513–0.753; $P < 0.05$) [Figure 2]. A survival analysis performed between the patients categorized into high (>9.87) and low (≤9.87) MELD-XI score groups showed that the patients with a high MELD-XI score (>9.87) had a significantly worse 1-year survival (log rank test; $P < 0.05$) [Figure 3].

Discussion

This study has some important findings. First, among patients with high-risk cardiac conditions who underwent elective or

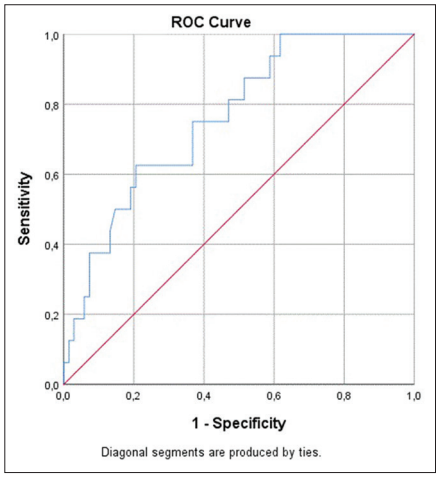

Figure 1: Receiver operating characteristic analysis of model for end-stage liver disease excluding international normalized ratio score for prediction of in-hospital mortality

Table 1: Overall characteristics of the study population (*n*=84)

Characteristics	Value
Age (years), median (IQR)	81 (18)
Sex (male), *n* (%)	41 (48.8)
Surgery type, *n* (%)	
General surgery	29 (34.5)
Genitourinary	15 (17.9)
Neurosurgery	6 (7.1)
Orthopedic	31 (36.9)
Vascular	3 (3.6)
High risk criteria, *n* (%)	
Severe valvular stenosis	15 (17.9)
Severe pulmonary hypertension	14 (16.7)
Serious ventricular arrhythmias	3 (3.6)
Supraventricular arrhythmias and AF with rapid ventricular response	19 (22.6)
Uncontrolled/severe angina pectoris	7 (8.3)
Recent/ongoing acute coronary syndrome	7 (8.3)
Multiple prosthetic heart valves	3 (3.6)
Decompensated/low-output heart failure	19 (22.6)
Diabetes mellitus, *n* (%)	37 (44.0)
Type 1	2 (2.4)
Type 2	35 (41.7)
Dietary therapy	8 (9.5)
Oral antidiabetics	15 (17.9)
Insulin	12 (14.3)
Hypertension, *n* (%)	73 (86.9)
Dietary controlled	7 (8.3)
Beta-blocker	44 (52.4)
Dihydropyridine calcium channel blocker	46 (54.8)
Non-dihydropyridine calcium channel blocker	17 (20.2)
ACEI/ARB	39 (46.4)
Nitrate	18 (21.4)
Diuretic	56 (6.7)
Alpha blocker	22 (26.2)
Hyperlipidemia, *n* (%)	22 (26.2)
Statin use	11 (13.1)
History of CVA/TIA, *n* (%)	12 (14.3)
History of chronic renal disease (stage 3 or higher), *n* (%)	21 (25.0)
On hemodialysis	4 (4.8)
Not on hemodialysis	17 (20.2)
History of chronic liver disease	4 (4.8)
History of heart failure, *n* (%)	42 (50)
Reduced ejection fraction (LVEF <50%)	12 (14.3)
Preserved ejection fraction (LVEF ≥50%)	30 (35.7)
Decompensated heart failure, *n* (%)	11 (13.1)
History of smoking, *n* (%)	29 (34.5)
Coronary artery disease	47 (56)
History of coronary bypass surgery	14 (16.7)
History of PTCA/stenting	13 (15.5)
Medical therapy	20 (23.8)
Peripheral arterial disease, *n* (%)	11 (13.1)
Carotid artery disease	3 (3.6)
Lower extremity arterial disease	3 (3.6)
Renal artery disease	1 (1.2)
Mesenteric vascular disease	1 (1.2)
Other	3 (3.6)
COPD, *n* (%)	18 (21.4)
Cancer, *n* (%)	15 (7.9)
Pulmonary hypertension, *n* (%)	14 (16.7)
Cardiac valvular disease	
Aortic stenosis (moderate-to-severe)	10 (11.9)
Severe	6 (7.1)
Mitral stenosis (moderate-to severe)	5 (6.0)
Severe	2 (2.4)
Other (tricuspid, pulmonary stenosis or any valvular insufficiency greater than mild degree)	10 (11.9)
Prosthetic cardiac valve, *n* (%)	6 (7.1)
Aortic	2 (2.4)
Mitral	2 (2.4)
Multi-prosthesis	2 (2.4)
Atrial fibrillation, *n* (%)	17 (20.2)
Newly diagnosed	4 (4.8)
Paroxysmal	6 (7.1)
Persistent	1 (1.2)
Permanent	6 (7.1)
Other supraventricular arrhythmia, *n* (%)	8 (9.5)
Atrial tachycardia	2 (2.4)
Atrial flutter	5 (6.0)
AVNRT/AVRT	1 (1.2)
Ventricular arrhythmia, *n* (%)	3 (3.6)
Ventricular tachycardia	1 (1.2)
Ventricular fibrillation	0 (0)
Frequent VPCs (>500 VPCs/h)	2 (2.4)
Implantable cardiac electronic device, *n* (%)	
Pacemaker (single chamber/dual chamber)	0 (0)
ICD	1 (1.2)
CRT-P/CRT-D	0 (0)
Anticoagulant use, *n* (%)	18 (21.4)
NOAC	9 (10.7)
Warfarin	7 (8.3)
LMWH/UFH	2 (2.4)
Laboratory data	
Creatinine(mg/dL), median-IQR	1.18 (0.79)
Total bilirubin (mg/dL), median-IQR	1.0 (1.3)
Hemoglobin (g/dL), mean±SD	11.7±2.1
White blood cell count (10^3/μL), median-IQR	9.39 (5.76)
Thrombocyte count (10^3/μL), median-IQR	232 (134)
CRP (mg/dL), median-IQR	49.8 (92.1)
Sodium (mEq/L), median-IQR	136 (5)
Potassium (mEq/L), median-IQR	4.1 (1.0)
ALT (U/L), median-IQR	14.0 (10.3)
AST (U/L), median-IQR	25.5 (18.0)
Left ventricular ejection fraction (%), median-IQR	50 (20)
ST segment depression greater than 1 mm on 12-lead ECG, *n* (%)	5 (7.4)

IQR: Interquartile range, ACEI/ARB: Angiotensin-converting enzyme inhibitor/angiotensin receptor blocker, CVA: Cerebrovascular accident, TIA: Transient ischemic attack, PTCA: Percutaneous transluminal coronary angioplasty, COPD: Chronic obstructive pulmonary disease, AVNRT: Atrioventricular nodal reentrant tachycardia, AVRT: Atrioventricular reentrant tachycardia, ICD: İmplantable cardioverter defibrillator, CRT-D: Cardiac resynchronization therapy with defibrillator backup, CRT-P: Cardiac resynchronization therapy without defibrillator backup, VPC: Ventricular premature complexes, LMWH: Low-molecular-weight heparin, UFH: Unfractionated heparin, NOAC: New oral anticoagulants, CRP: C- Reactive protein, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase

Table 2: Number of in-hospital cardiac adverse events and deaths by underlying disorder

Cardiac adverse event	In-hospital cardiac adverse events, *n* (%)	In-hospital cardiac deaths, *n* (%)
Perioperative ischemia and/or infarction	14 (16.7)	6 (7.1)
Pulmonary thromboembolism	6 (7.1)	4 (4.8)
Ventricular fibrillation preceded by monomorphic and polymorphic ventricular tachycardia	2 (2.4)	2 (2.4)
Asystole	2 (2.4)	1 (6.3)
High-grade atrioventricular block	2 (2.4)	1 (6.3)
Supraventricular tachycardia with rapid ventricular response	6 (7.1)	0 (0)
Decompensated/low-output heart failure	8 (9.5)	2 (2.4)

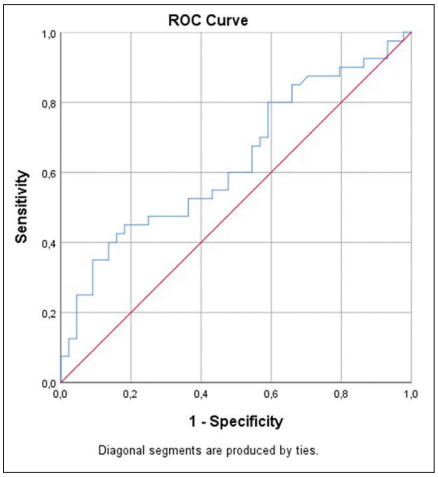

Figure 2: Receiver operating characteristic analysis of model for end-stage liver disease excluding international normalized ratio score for prediction of 1-year all-cause mortality

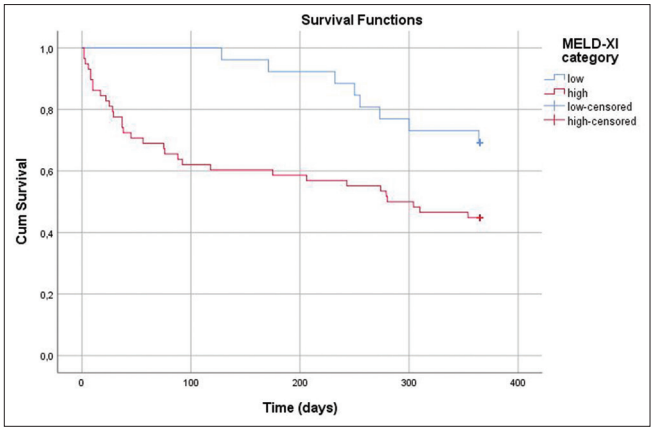

Figure 3: Kaplan–Meier curve of 1-year survival based on model for end-stage liver disease excluding international normalized ratio category (>9.87 vs. ≤9.87)

urgent noncardiac surgery, MELD-XI score was significantly higher in those with in-hospital cardiac and 1-year all-cause mortality compared to survivors. Second, MELD-XI score independently predicted in-hospital cardiac mortality and 1-year all-cause mortality. Collectively, these results suggest that MELD-XI score is a useful score for predicting prognosis after both elective and urgent noncardiac surgery among patients with high-risk cardiac conditions.

Cardiac risk is an important aspect of noncardiac surgery for both surgeons and patients.[17,18] On average, 7%–11% of all noncardiac surgical operations are complicated, and mortality rates range between 0.8% and 1.5%,[17] with as much as 42% of all complications being of cardiac origin.[18] Apart from emergent or cardiovascular procedures, several cardiac conditions increase the risk of a noncardiac procedure.[1] However, not all high-risk patients die from or suffer adverse cardiovascular events, with other procedural, anesthetic, and patient-specific factors being operational in the perioperative period or in the long term. Although some high-risk cardiac conditions may be treated and cardiac risk may be reduced,[19-34] such procedures may not be performed due either to urgency of surgery or presence of multiple/severe comorbidities. Hence, other prognostic tools for advanced risk stratification of patients undergoing noncardiac surgery are needed.

MELD score was originally developed to predict clinical outcomes in liver disease.[4] It was subsequently used in various cardiac conditions.[7-9] The suggested mechanism by which MELD score predicts mortality in cardiac conditions is reduced forward cardiac output and end-organ perfusion (forward failure) as well as increased central venous pressure leading to hepatic and renal venous congestion (backward failure), which are reflected by increased serum creatinine, total bilirubin, and INR.[35-37] MELD-XI score, a modification of the original MELD score excluding INR from the model, was developed to determine the prognosis of patients using anticoagulants. MELD-XI score has been successfully tested in various cardiac conditions[11-16] and critically ill.[38] Although MELD-XI score was tested in cardiac surgery and cardiac transplantation,[11,12,16,39] our study is the first to investigate it for advanced risk stratification of high-risk cardiac patients undergoing noncardiac surgery.

In the present study, MELD-XI score successfully independently predicted both in-hospital cardiac mortality and 1-year all-cause mortality. It was also highly correlated with revised cardiac risk index (Lee) score, which has been shown to accurately predict perioperative cardiac events.[3] When hemodynamic burden of conditions requiring noncardiac surgery is added to high-risk cardiac conditions, overt or subclinical heart failure may develop, resulting in an elevated MELD-XI score. Hence, a higher MELD-XI score in high-risk surgical patients may indicate an even

Table 3: Comparison of demographic, clinical, and cardiac and biochemical variables between the study groups with and without in-hospital cardiac mortality

Variable	In-hospital cardiac mortality (+) (*n*=16)	In-hospital cardiac mortality (−) (*n*=68)	*P*
Sex (male), *n* (%)	6 (37.5)	35 (51.5)	0.23*
Age (years), median-IQR	79 (18)	82 (17)	0.50[α]
Surgery type, *n* (%)			
General surgery	5 (31.3)	24 (35.3)	0.73*
Genitourinary	2 (12.5)	13 (19.1)	0.12**
Neurosurgery	3 (18.8)	3 (4.4)	0.067**
Orthopedic	6 (37.5)	25 (36.8)	0.86*
Vascular	0 (0)	3 (4.4)	0.23**
Diabetes mellitus, *n* (%)	9 (56.3)	28 (41.2)	0.40*
Hypertension, *n* (%)	16 (100)	57 (83.8)	0.11*
Hyperlipidemia, *n* (%)	4 (25)	18 (26.5)	0.59**
Cerebrovascular accident, *n* (%)	2 (12.5)	10 (14.7)	0.14**
Coronary artery disease, *n* (%)	11 (68.8)	36 (52.9)	0.26*
Peripheral artery disease, *n* (%)	1 (6.25)	10 (14.7)	0.37**
Angina pectoris, *n* (%)	4 (25)	3 (4.4)	0.03**
Heart failure, *n* (%)	8 (50)	34 (50)	1.00*
Chronic renal disease (Stage 3 or higher), *n* (%)	3 (18.8)	18 (26.5)	0.49**
Chronic liver disease, *n* (%)	1 (6.25)	3 (4.4)	0.10**
COPD, *n* (%)	3 (18.8)	16 (23.5)	0.38**
Pulmonary hypertension, *n* (%)	3 (18.8)	11 (16.2)	0.47**
Severe aortic/mitral stenosis, *n* (%)	2 (12.5)	6 (8.8)	0.31**
Prosthetic heart valves, *n* (%)	1 (6.25)	5 (7.4)	0.53**
Cancer, *n* (%)	4 (25.0)	11 (16.2)	0.25**
Ventricular arrhythmia, *n* (%)	1 (6.25)	2 (2.9)	0.45**
Supraventricular arrhythmia including AF, *n* (%)	6 (37.5)	19 (27.9)	0.17*
Implantable cardiac electronic devices, *n* (%)	0 (0)	1 (1.5)	0.36**
Anticoagulant use, *n* (%)	3 (18.8)	15 (22.1)	0.11**
Beta-blocker use, *n* (%)	4 (25.0)	40 (58.8)	0.039**
Statin use, *n* (%)	2 (12.5)	9 (13.2)	0.82**
History of smoking, *n* (%)	5 (31.3)	24 (35.3)	0.67*
ST depression >1 mm, *n* (%)	4 (25)	14 (20.6)	0.34**
Left ventricular ejection fraction (%), median-IQR	45 (34)	50 (19)	0.98[α]
Serum sodium (mEq/L), median-IQR	136.0 (6.0)	136.0 (4.0)	0.96[α]
Serum potassium (mEq/L), median-IQR	4.32 (0.53)	4.10 (1.10)	0.09[α]
Hemoglobin (g/dL), mean±SD	10.45 ±1.67	11.89 ±3.30	0.039[¶]
White blood cell count, median-IQR	8.92 (7.20)	9.57 (5.60)	0.43[α]
Serum creatinine (mg/dL), median-IQR	1.73 (2.20)	1.16 (0.67)	0.003[α]
Serum total bilirubin (mg/dL), median-IQR	1.04 (1.28)	1.00 (1.26)	0.86[α]
Serum CRP (mg/dL), median-IQR	35.9 (147.2)	58.3 (90.3)	0.38[α]
Serum AST (U/L), median-IQR	21.0 (19.0)	27.0 (16.0)	0.32[α]
Serum ALT (U/L), median-IQR	14.0 (12.0)	15.0 (10.0)	0.64[α]
INR, median-IQR	1.28 (0.88)	1.18 (0.26)	0.28[α]
Revised cardiac risk index (Lee) score, median-IQR	3 (3)	2 (1)	0.034[α]
MELD-XI score, median-IQR	12.23 (6.53)	9.66 (3.81)	0.001[α]

*Chi-square test, **Fisher's exact test, [α]Mann–Whitney-U-test, [¶]Independent samples *t*-test. COPD: Chronic obstructive pulmonary disease, CRP: C-reactive protein, SD: Standard deviation, INR: International normalized ratio, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, MELD: Model for end-stage liver disease, IQR: Interquartile range

higher cardiac risk. Of note, our study found that MELD-XI score was not correlated with echocardiographic left ventricular ejection fraction (LVEF). However, heart failure may develop in patients with normal LVEF. In support of this view, MELD-XI score was positively correlated with the rates of heart failure (combination of diastolic and systolic failure). In addition, it was significantly and positively correlated with coronary artery disease, severe valvular lesions, and ST segment depression and significantly and negatively correlated with serum hemoglobin count, all of which may also be responsible for cardiovascular dysfunction.

Table 4: Comparison of demographic, clinical, biochemical, and cardiac testing variables and model for end-stage liver disease -XI score in patients with and without 1-year mortality

Variable	1-year all-cause mortality (+) (*n*=40)	1-year all-cause mortality (−) (*n*=44)	*P*
Sex (male), *n* (%)	17 (42.5)	24 (54.5)	0.19*
Age (years), median (IQR)	79 (22)	82 (15)	0.95*
Surgery type, *n* (%)			
General surgery	13 (32.5)	16 (36.4)	0.38*
Genitourinary	5 (12.5)	10 (22.7)	0.46*
Neurosurgery	4 (10.0)	2 (4.6)	0.11**
Orthopedic	17 (42.5)	14 (31.8)	0.65*
Vascular	1 (2.5)	2 (4.6)	0.92**
Diabetes mellitus, *n* (%)	19 (47.5)	18 (40.9)	0.35*
Hypertension, *n* (%)	34 (85)	39 (88.6)	0.43*
Hyperlipidemia, *n* (%)	8 (20.0)	14 (31.8)	0.16*
Cerebrovascular accident, *n* (%)	5 (12.5)	7 (15.9)	0.22*
Coronary artery disease, *n* (%)	20 (50.0)	27 (61.4)	0.47*
Peripheral artery disease	5 (12.5)	6 (13.6)	0.88*
Angina pectoris, *n* (%)	4 (10.0)	3 (6.8)	0.11**
Heart failure, *n* (%)	18 (45.0)	24 (54.5)	0.35*
Chronic renal disease (Stage 3 or higher), *n* (%)	9 (22.5)	12 (27.3)	0.67*
Chronic liver disease, *n* (%)	2 (5.0)	2 (4.6)	0.88**
COPD, *n* (%)	9 (22.5)	10 (22.7)	0.91*
Pulmonary hypertension, *n* (%)	9 (22.5)	5 (11.4)	0.04*
Severe aortic/mitral stenosis, *n* (%)	4 (10.0)	4 (9.1)	0.92**
Prosthetic heart valves, *n* (%)	0 (0)	6 (13.6)	0.06**
Cancer, *n* (%)	8 (20.0)	7 (15.9)	0.43*
Ventricular arrhythmia, *n* (%)	2 (5.0)	1 (2.3)	0.25**
Supraventricular arrhythmia including AF, *n* (%)	10 (25.0)	15 (34.1)	0.08*
Implantable cardiac electronic devices, *n* (%)	1 (2.5)	0 (0)	0.37**
Anticoagulant use, *n* (%)	7 (17.5)	11 (25.0)	0.41*
Beta-blocker use, *n* (%)	18 (45)	26 (59.1)	0.26*
Statin use, *n* (%)	3 (7.5)	8 (18.2)	0.43**
History of smoking, *n* (%)	12 (30.0)	17 (38.6)	0.22*
ST segment depression >1 mm, *n* (%)	4 (10.0)	1 (2.3)	0.07**
Left ventricular ejection fraction (%), median-IQR	45 (27)	54 (18)	0.11[α]
Serum sodium (mEq/L), median-IQR	135.0 (5.0)	136.0 (4.0)	0.54[α]
Serum potassium (mEq/L), median-IQR	4.30 (0.80)	4.10 (1.10)	0.48[α]
Hemoglobin (g/dL), mean±SD	11.21 ±2.32	11.95±1.88	0.046[¶]
White blood cell count, median-IQR	9.48 (6.40)	9.29 (4.63)	0.40[α]
Serum creatinine (mg/dL), median-IQR)	1.24 (1.17)	0.90 (0.67)	0.12[α]
Serum total bilirubin (mg/dL), median-IQR)	1.04 (4.52)	0.89 (0.87)	0.74[α]
Serum CRP (mg/dL), median-IQR)	43.57 (105.14)	63.12 (91.60)	0.93[α]
Serum ALT (U/L), median-IQR)	14.00 (11.00)	16.00 (10.00)	0.26[α]
Serum AST (U/L), median-IQR)	22.00 (18.00)	27.0 (16.00)	0.036[α]
INR	1.22 (0.31)	1.18 (0.33)	0.981[α]
Revised cardiac risk index (Lee) score, median-IQR	2 (2)	1.5 (1)	0.141[α]
MELD-XI score, median-IQR	10.80 (6.31)	9.70 (3.70)	0.037[α]

*Chi-square test, **Fisher's exact test, [α]Mann–Whitney U-test. COPD: Chronic obstructive pulmonary disease, CRP: C-reactive protein, SD: Standard deviation, INR: International normalized ratio, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, MELD: Model for end-stage liver disease, IQR: Interquartile range

Various studies have reported a range of MELD-XI scores for mortality prediction, and this variability may stem from different inclusion criteria and conditions. We found a MELD-XI cutoff point of 10.70 for in-hospital cardiac mortality, which is in agreement with an almost identical score reported by He *et al*.[13] However, Wernly *et al*.[10] and Critsinelis *et al*.[11] reported much higher cutoff points (12 and 14, respectively) for in-hospital mortality among patients with critical illness and those undergoing LVAD implantation, respectively. Similarly, our MELD-XI cutoff point of 9.87 for long-term all-cause mortality is much lower than those reported by Yang *et al*.[14] and Spieker *et al*.[12] (17 and 16, respectively) after LVAD

placement and percutaneous mitral valve repair, respectively. He *et al*.[13] and Wernly *et al*.[10] reported somewhat lower, albeit still higher, cutoff points (13 and 12, respectively) for prediction of long-term mortality after infective endocarditis and critical illness, respectively. According to our opinion, our MELD-XI cutoff points were lower than previously reported because our patients were at the highest risk of death caused by the risk of noncardiac surgery added to cardiac high-risk conditions, a higher median age (81 years) and a higher rate of heart failure (50%). Hence, lower MELD-XI scores may have predicted short-term and long-term mortality among our patients.

Limitations

This study had some limitations. First, it had a retrospective design. Second, the study population was relatively small because a sizeable portion of patients having high-risk cardiac conditions refuse to undergo noncardiac surgery due to heightened cardiac risk, or some surgeons refuse to operate such patients, particularly when there is no compelling indication for surgery. Furthermore, corrective or palliative cardiac procedures are performed prior to noncardiac surgery in some of patients with high-risk cardiac conditions. Third, we only took into consideration high-risk cardiac conditions; thus, it is unclear how noncardiac factors affected mortality rates. Fourth, although MELD-XI score gives an estimation of both renal and hepatic function, we also did not seek to answer whether MELD-XI score can predict all-cause in-hospital mortality. Fifth, since we only included in-hospital cardiac mortality, 1-year all-cause mortality rate did not include in-hospital noncardiac mortality. Therefore, 1-year all-cause mortality rate was in fact a combination of in-hospital cardiac and postdischarge all-cause mortality rates, which may have created heterogeneity.

Conclusion

MELD-XI score was predictive of in-hospital cardiac and 1-year all-cause mortality independently of high-risk cardiac factors among patients undergoing elective or urgent noncardiac surgery. Hence, MELD-XI score was able to further risk stratify noncardiac surgical candidates which are already at high cardiac risk. This score's role in perioperative risk estimation should be further evaluated by randomized controlled studies.

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Conflicts of interest

There are no conflicts of interest.

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