MELD-XI Score in Hospitalized Heart Failure Patients with Cardiac Electronic Devices

Kardiyak Elektronik Cihazları olan Hospitalize Edilmiş Kalp Yetersizliği Hastalarında MELD-XI Skoru

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ABSTRACT

Objective: MELD-XI (Model for End-Stage Liver Disease Excluding INR) score predicts mortality in patients with heart failure. Herein, we assessed the role of MELD-XI score in predicting in-hospital mortality among heart failure patients having intracardiac cardioverter defibrillator (ICD) or cardiac resynchronization therapy with defibrillator backup (CRT-D) who presented with appropriate device shock or acute decompensated heart failure.

Methods: We reviewed the medical records of patients with implantable cardioverter defibrillator or cardiac resynchronization therapy with defibrillator backup admitted to coronary care unit with acute decompensated heart failure or appropriate implantable device shocks between 01 January 2013 and 01 November 2018. MELD-XI score was compared between the deceased and surviving patients. The correlation of MELD-XI score with in-hospital mortality was sought.

Results: There were 106 coronary care unit admissions of 67 patients (52 (77.6%) males and 15 (22.4%) females), who had a mean age of 64.8 (range 19-93) years. Eighty-eight (83.0%) admissions were for acute decompensated heart failure and 18 (17.0%) for appropriate device shock and/or electrical storm. A total of 16 (15.1%) patients died at hospital. The median MELD-XI score of the patients who died at hospital was significantly greater than that of the survivors (11.80 (0.59-28.98) vs 15.24 (9.11-24.64); p<0.05). A binary logistic regression analysis showed that MELD-XI score was a significant independent predictor of in-hospital mortality (X²=1.229 (%95 CI 1.06-1.43); p<0.05).

Conclusion: MELD-XI score successfully predicts in-hospital mortality among patients with ICD or CRT-D admitted with acute decompensated heart failure or appropriate implantable electronic device shocks.

Key Words: MELD-XI, heart failure, electrical storm, shock, implantable cardioverter-defibrillator, cardiac resynchronization therapy

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ÖZET

Amaç: MELD-XI (Model for End-Stage Liver Disease Excluding INR- INR’yi Dilşeyen Son Dönem Karaciğer Hastalığı Modeli) kalp yetersizliği hastalarında mortaliteyi öngörmektedir. Bu çalışmada, implantede edilir kardiyoverter defibrilatör (ICD) ya da defibrilatör destekli kardiyak resenkronizasyon tedavisi (CRT-D) olan ve uygun cihaz şoku ya da akut dekompanse kalp yetersizliği ile başvuran kalp yetersizliği hastalarında hastane içi mortaliteyi öngörmeye MELD-XI skorunun rolünü değerlendirildik.

Yöntem: Bu çalışmada, implantede edilir kardiyoverter defibrilatör ya da defibrilatör destekli kardiyak resenkronizasyon tedavisi olan ve 01 Ocak 2013 ile 01 Kasım 2018 tarihleri arasında koroner bakım ünitesine akut dekompanse kalp yetersizliği ya da uygun cihaz şoku ile başvuran hastaların tıbbi kayıtlarını gözden geçirdik. MELD-XI skoru ölen ve yaşayan hastalar arasında karşılaştırıldı.

Bulgular: Ortalamalı yaşlan 64,8 (aralık 19-93) yıl olan toplam 67 (52 (%77,6) erkek, 15 (22,4) kadın) hastanın toplam 106 koroner bakım ünitesi yatışı vardır. Seksen sekiz (%83,0) yatış akut dekompanse kalp yetersizliği ve 18 (%17,0) yatış uygun cihaz şoku ve veya elektriksel fırıncı nedeniyle yapılmıştır. Toplamda 16 (%15,1) hastane yaşamı sona ermiştir. Hastaneden ölen hastaların ortanca MELD-XI skoru 11.80 (0.59-28.98)’e karşılık 15.24 (9.11-24.64); p<0.05) bir lojistik regresyon analizi MELD-XI skoru hastanecik mortaliteyi bağımsız öngörücü olduğu gösterildi (X²=1.229 (%95 CI 1.06-1.43); p<0.05).

Sonuç: MELD-XI skoru ICD ya da CRT-D’si olup akut dekompanse kalp yetersizliği ya da uygun implantede edilir elektriksel cihaz şoku ile başvuran hastalarda hastane içi mortaliteyi bağımsızla öngörmektir.

Anahtar Sözcükler: MELD-XI, kalp yetersizliği, elektriksel fırtına, şok, implantede edilir kardiyoverter-defibrilatör, kardiyak resenkronizasyon tedavisi

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INTRODUCTION

It has been recently postulated that hepatic and/or renal affection by acute cardiac conditions such that heart failure and low cardiac output may predict survival among critically ill patients and risk stratify them, mainly occurring due to hyperperfusion, venous congestion, or both (1-5). As such, increased serum total bilirubin is known to be linked with hepatocellular hypoxia originating from low cardiac output and/or increased hepatic venous pressure (1,6). This link between poor cardiac function, mainly in the form of lowered cardiac output with venous congestion and hepatic and renal derangements, has led to a search for hepatic and renal surrogate markers of cardiac dysfunction and its prognosis. So, the original Model for End-Stage Liver Disease (MELD) score has been developed as a tool to predict clinical outcomes in patients with liver disease. It involves the logarithmic conversions of serum creatinine, total serum bilirubin, and International Normalized Ratio (INR) and calculated as 0.957 x ln(Serum Cr) + 0.378 x ln(Serum Bil) + 1.120 x ln(INR) + 0.643 x 10 (if hemodialysis, value for creatinine is automatically set to 4.0) (7). It was considered a good indicator of the severity of hepatic disorders in patients on liver transplant waiting list (8) and those with multi-organ failure (9). Additionally, it was shown to offer prognostic implications for patients with heart failure (10) and patients who were implanted left ventricular assist devices (LVADs) (11,12). The MELD score’s ability for prediction of prognosis in heart failure stems from its capacity to reflect hepatic and renal disturbances in low-output and/or venous congestive conditions (13).

The use of MELD, however, can be problematic in a significant proportion of patients with congestive heart failure or LVADs who are on systemic anticoagulants that cause INR elevation beyond that observed in hepatic congestion/dysfunction, and also among those who are on warfarin or phenprocoumon. For this purpose, MELD-XI score excluding INR has been developed (14) as a modification of the original MELD score, and was shown to be as accurate as its predecessor for estimating mortality in liver cirrhosis (14).

To date, MELD-XI score has been shown to predict survival in a number of cardiac conditions including heart failure and after cardiac transplantation (14-17) but it has not been used for patients with cardiac implantable electrical defibrillator hospitalized for decompensated heart failure and implantable electronic cardiac device shock/electrical storm. In this study we aimed to investigate the role of MELD-XI score in predicting in-hospital mortality among patients with implantable cardioverter-defibrillator (ICD) or cardiac resynchronization therapy with defibrillator backup (CRT-D) who presented with device shock/electrical storm or acute decompensated heart failure.

MATERIALS and METHOD

This study was approved by Başkent University Institutional Review Board (Project no:KA19/57) and supported by Başkent University Research Fund. We reviewed the medical records of all heart failure patients with implantable cardioverter-defibrillators (ICD) or cardiac resynchronization therapy with defibrillator (CRT-D) who presented to Başkent University Faculty of Medicine Department of Cardiology, Coronary Care Unit with decompensated heart failure or device shock/electrical storm upon their implanted device type (CRT-D vs ICD subgroups) and their mortality. The exclusion criteria were as follows: patients who were admitted for decompensated heart failure and device shock/electrical storm, there were a total of 156 admissions in this category. Admission of patients and admissions meeting the exclusion criteria, a total of 67 patients admitted in a total of 106 admissions remained for the final analysis (Figure 1-study flow chart). Among these, in-hospital mortality was determined. The MELD-XI score was then compared between patients who died at hospital (i.e having in-hospital mortality) versus who survived. The patients were then subgrouped based upon their implanted device type (CRT-D vs ICD subgroups) and their indication for coronary care unit admission (decompensated heart failure vs device shock/electrical storm), and the MELD-XI score was compared between the deceased and survived patients in each subgroup.

Figure 1: Study flow chart

All coronary care unit Admissions of patients with ICD/CRT-D between 1 January 2013 and 1 November 2018 (n=212)

Coronary care unit admissions for decompensated heart failure or device shock/electrical storm (n=156)

Admissions enrolled (n=106 in 67 patients)

Patients that died at hospital (n=16)

Admissions excluded due to meeting the exclusion criteria (n=50)

Patients that survived the hospital stay (n=51)

Statistical analysis
All statistical analyses were performed using SPSS v.20 (SPSS Inc., Chicago, IL, USA) statistical software package. Normality of the distribution of quantitative variables was tested using Kolmogorov-Smirnov test. Descriptive statistics included mean±standard deviation for normally distributed quantitative variables, median (minimum-maximum for non-normally distributed quantitative variables, and number and percentage (%) for qualitative variables. The significance between the means of the quantitative variables was tested using independent samples’ t test for the normally distributed quantitative variables and Mann Whitney-U test for the non-normally distributed quantitative variables. Qualitative variables were compared using the Pearson Chi-square test or Fisher’s exact test. The significant predictors of in-hospital mortality were initially tested with a univariate analysis using all available demographic, clinical, biochemical, and echocardiographic variables.
and their mean age was 64.8±17.9 years. The heart failure etiology was ischemic cardiomyopathy in 43 (64.2%) patients, and nonischemic cardiomyopathy in 24 (35.8%) patients. The mean ejection fraction was 57%±14%.

Independent samples t test, ** Chi-Square test, *** Mann Whitney-U test
CAD: Coronary artery disease, CRT-D: Cardiac resynchronization therapy with defibrillator backup; ICD: implantable cardioverter defibrillator, MELD-XI: Model for end stage liver disease excluding international noralized ratio; ALT: alanine aminotransferase, AST: Aspartate aminotransferase, CRP: Carbon monoxide-reactive protein, ACEI: Angiotensin converting enzyme inhibitor, ARB: angiotensin receptor blocker, NOACs: Novel oral anticoaguant; QRS: QRS complex on 12-lead electrocardiogram

RESULTS
There were a total of 106 coronary care unit admissions of a total of 67 patients. Fifty-two (77.6%) patients were male and 15 (22.4%) were female, and their mean age was 64.8±17.9 years. The heart failure etiology was ischemic cardiomyopathy in 43 (64.2%) patients, and nonischemic cardiomyopathy in 24 (35.8%) patients. The mean ejection fraction was 27.3%±13.6%.

Table 1. Clinical, demographic, and biochemical characteristics of the study population

| Characteristics | Patients that died at hospital (n=16) | Patients that survived hospital stay (n=51) | p |
|-----------------|--------------------------------------|------------------------------------------|---|
| Age (years)     | 65.8±16.7                            | 56.4±19.3                                | >0.05*|
| Male, n (%)     | 13 (81.3%)                           | 40 (78.4%)                               | >0.05**|
| Hypertension, n (%) | 10 (62.5%) | 38 (74.5%)     | >0.05**|
| Diabetes mellitus, n (%) | 7 (43.8%) | 20 (39.2%)    | >0.05**|
| Smoking (active), n (%) | 2 (12.5%) | 6 (11.8%)     | >0.05**|
| CAD (all severities), n (%) | 13 (81.3%) | 37 (72.5%) | >0.05**|
| Cardiomyopathy type | Ischemic, n (%) | 10 (62.5%) | 33 (64.7%) | >0.05**|
| Non-ischemic, n (%) | 5 (31.3%) | 19 (37.3%)    | >0.05**|
| Implantable device subtype | CRT-D, n (%) | 5 (31.3%) | 20 (39.2%) | >0.05**|
| ICD, n (%)      | 7 (43.8%)                            | 35 (68.6%)                               | >0.05**|
| Primary prevention, n (%) | 9 (56.3%) | 22 (43.1%) | >0.05**|
| Secondary prevention, n (%) | 3 (18.8%) | 8 (15.7%) | >0.05**|
| Presentation type (all admissions, n=106) | Compensated heart failure, n (%) | 12 (75.0%) | 75 (83.3%) | >0.05**|
| Congestive symptoms, n (%) | 10 (62.5%) | 61 (67.7%) | >0.05**|
| Low output symptoms, n (%) | 2 (12.5%) | 18 (20.0%) | >0.05**|
| Device shock/electrical storm, n (%) | 3 (18.6%) | 14 (15.5%) | >0.05**|
| Device shock, n (%) | 3 (18.6%) | 11 (12.2%) | >0.05**|
| Electrical storm, n (%) | 0 (0%) | 3 (3.3%) | >0.05**|
| Duration of stay at coronary care unit (days) | 4 (2-72) | 6 (8-118) | >0.05**|
| MELD-XI score    | 15.24 (9.11-24.64)                    | 11.80 (0.59-28.98)                       | <0.05***|

Laboratory parameters
- Hb (g/dL): 11.7±4.8 vs. 12.8±5.6, <0.05*
- White blood cell (µL): 8.1±2.9 vs. 7.6±1.9, <0.05*
- Platelet (10³/µL): 236.4±55.7 vs. 255.6±32.2, <0.05*
- Creatinine (mg/dL): 1.46±0.5 vs. 1.33±0.9, <0.05*
- Blood urea nitrogen (BUN) (mg/dL): 25.8±12.3 vs. 22.4±10.8, <0.05*
- Na (mmol/L): 134.7±16.4 vs. 132.9±12.5, <0.05*
- K (mmol/L): 5.3±0.6 vs. 4.9±1.1, <0.05*
- Total bilirubin (mg/dL): 2.3±2.0 vs. 1.58±1.8, <0.05*
- ALT (U/L): 28.3±12.6 vs. 21±8.8, <0.05*
- AST (U/L): 30.4±11.8 vs. 34.4±9.7, <0.05*
- CRP (mg/dL): 23.6±10.7 vs. 10.8±8.9, <0.01*

Medications
- Beta blocker, n (%): 13 (81.3%) vs. 40 (78.4%), >0.05**
- ACEI/ARB, n (%): 12 (75.0%) vs. 42 (82.4%), >0.05**
- Statin, n (%): 10 (62.5%) vs. 41 (80.4%), >0.05**
- Amiodarone, n (%): 5 (31.3%) vs. 13 (25.5%), >0.05**
- Loop diuretic, n (%): 14 (87.5%) vs. 40 (78.4%), >0.05**
- Aldosterone antagonist, n (%): 10 (62.5%) vs. 24 (47.1%), >0.05**
- Antiplatelet agents, n (%): 12 (75.0%) vs. 42 (82.4%), >0.05**
- Anticoagulant (warfarin, heparin, NOACs), n (%): 7 (43.8%) vs. 20 (39.2%), >0.05**

Echocardiographic and electrocardiographic parameters
- Left ventricular ejection fraction (%): 27.3±13.6 vs. 24.3±10.9, >0.05*
- Left ventricular end-systolic diameter (mm): 45.5±18.6 vs. 46.5±16.6, >0.05*
- Left ventricular hypertrophy (any wall thickness >11 mm), n (%): 66.8±16.7 vs. 64.8±13.0, >0.05*
- Left ventricular diastolic dysfunction (any degree), n (%): 10 (62.5%) vs. 40 (78.4%), <0.05**
- Sinus Rhythm: 10 (62.5%) vs. 40 (78.4%), <0.05**
- Atrial fibrillation: 14 (87.5%) vs. 60 (89.6%), >0.05**
- Paced (biventricular or right ventricular): 10 (62.5%) vs. 30 (58.8%), >0.05**
- Native QRS width: 3 (18.8%) vs. 11 (21.6%), >0.05**
- QRS duration: 3 (18.8%) vs. 6 (11.8%), >0.05**
- QRS duration: 116±24.8 vs. 113±18.8, >0.05**

All univariate predictors of in-hospital mortality with p value < 0.25 were then used in a binary logistic regression model to determine the independent predictors in-hospital mortality. Receiver Operating Characteristics (ROC) analysis was performed to determine the predictive ability of MELD-XI score for prediction of in-hospital mortality.
The indication for device implantation was progressive heart failure symptoms in 25 (37.3%) patients (the CRT-D implanted patients); primary prevention of malignant ventricular arrhythmias in 31 (46.3%) patients (the patients with ICD implanted for primary prevention); and secondary prevention of malignant ventricular arrhythmias in 11 (16.4%) patients (the patients with ICD implanted for secondary prevention). Eighty-eight (83.0%) hospital admissions were for decompensated acute heart failure and 18 (17.0%) for appropriate device shock and/or electrical storm.

The appropriate device shocks and/or electrical storms occurred due to stable monomorphic VT in 8 patients, polymorphic VT due to magnesium depletion in 1 patient, pulmonary, urinary or other infections in 2 patients, ischemia in 1 patient, acute COPD exacerbation in 1 patient, and decompensated heart failure in 5 patients. The comparison of demographic, biochemical, echocardiographic, and electrocardiographic characteristics between deceased and surviving patients were presented on Table 1.

The median hospital stay was 6 (min 2-max 118) days. The patients with CRT-D significantly more commonly presented with decompensated heart failure than those with ICD (94.3% vs 77.5%, p<0.05). In contrast, patients with ICDs more commonly presented with device shock/electrical storm than those with CRT-D (22.5% vs 5.7%, p<0.05). A total of 16 (23.8%) patients died at hospital.

The mean MELD-XI score was 12.78±5.80. The median MELD-XI score of patients that died at hospital was significantly greater than those who survived (15.24 (9.11-24.64) vs 11.80 (0.59-28.98); p<0.05). When the patients were subgrouped into CRT-D and ICD subgroups based on the implanted device type, there was a significant difference between the MELD-XI scores of those that died at hospital and those that survived within the CRT-D subgroup (20.05 (13.92-20.69) vs 13.05 (2.71-27.17); p<0.05) but not within the ICD subgroup (14.58±5.20 vs 11.46±5.84; p>0.05). A similar subgroup analysis was performed on the basis of the indication for hospital admission among the subgroup of patients hospitalized for decompensated heart failure, showing that MELD-XI score was significantly greater in those who died at hospital compared to those who survived (15.68±4.75 vs 12.21±6.13). Among patients with appropriate device shocks or electrical storm, the MELD-XI score could not be compared as there was only one patient who died in the device shock/electrical storm subgroup (Table 2).

Univariate analysis of in-hospital mortality showed that MELD-XI score was a significant univariate predictor of in-hospital mortality (p<0.05) along with age (p<0.05), serum creatinine (p<0.05), admission CRP (p<0.05), and admission systolic blood pressure (p<0.05). A binary logistic regression analysis showed that MELD-XI score was a significant independent predictor of in-hospital mortality (X²=12.3 (95% CI 1.06-1.43); p<0.05). A ROC analysis performed to determine the predictive ability of the MELD-XI score for in-hospital mortality revealed that a MELD-XI score of ≥13.88 significantly predicted in-hospital mortality with a sensitivity 68.8%, a specificity of 65.6%, a positive predictive value of 92.2% and a negative predictive value of 26.2% (AUC= 0.695 (95% CI 0.57-0.82); p<0.05) (Figure 2). A categorization according to the MELD-XI score was also performed, in which patients with a MELD-XI score of <13.88 were categorized as the low MELD-XI score group and the ones with a MELD-XI score of ≥13.88 as the high MELD-XI score group. There was a significantly worse in-hospital survival among patients with a high MELD-XI score (Log Rank (Mantel-Cox) test; p<0.05) (Figure 3).

Table 2. Inter-group and intra-group comparisons of the MELD-XI score between patients with and without in-hospital mortality

| In-hospital mortality in the general patient population | Deceased | Survived | p    |
|---------------------------------------------------------|----------|----------|------|
| In-hospital mortality among patients with CRT-D         | 15.24 (9.11-24.64) | 11.80 (0.59-28.98) | <0.05* |
| In-hospital mortality among patients with ICD           | 20.05 (13.92-20.69) | 13.05 (2.71-27.17) | <0.05* |
| In hospital mortality among patients with decompensated heart failure | 13.73 (9.11-24.64) | 10.71 (0.49-28.98) | >0.05* |
| In hospital mortality among patients with decompensated heart failure | 15.22 (9.11-24.64) | 11.99 (0.59-28.98) | >0.05* |

* Mann Whitney-U test, CRT-D: Cardiac resynchronization therapy with defibrillator backup; ICD: implantable cardioverter defibrillator

Figure 2. ROC curve of the MELD-XI score for the prediction of in-hospital mortality
Hepatic and/or renal functional impairment mainly secondary to hypoperfusion, venous congestion, or both as a result of acute or chronic cardiac dysfunction such as heart failure and low cardiac output may predict survival among critically ill patients (1-5). Increased serum total bilirubin and creatinine are known to be linked with hepatocellular and renal hypoxia and venous congestion originating from low cardiac output and/or increased venous pressure (1,6,18) Therefore, it is plausible that changes in serum levels of both parameters reflect worsening cardiac function. This link between poor cardiac function and hepatic and renal derangement prompted a search for hepatic and renal surrogate markers of cardiac dysfunction and its prognosis.

As a result, the original MELD score and its modification MELD-XI score have been developed, both of which have been validated for use to predict mortality risk in heart failure and other cardiac conditions as well as patients undergoing cardiac surgery including cardiac transplantation and left ventricular assist device implantation (19-24). However, neither score has been used for patients with cardiac implantable electrical devices hospitalized for decompensated heart failure and implantable electronic device shock/electrical storm. To our best knowledge, our study demonstrated to the first time in the medical literature that MELD-XI score can be used as a predictor of in-hospital mortality among patients with CRT-D or ICD that presented with either decompensated heart failure or device shock or electrical storm. While previous studies have reported that MELD-XI score may predict both short and long-term prognosis in various patient populations (13-15,22,23,25,26), we demonstrated that a cut-off value of ≥13.88 for MELD-XI score was associated with a significant risk of in-hospital mortality with a relatively fair sensitivity and specificity. Moreover, a high-MELD-XI category significantly worsened in-hospital survival. Critsinelis et al (16) reported an almost identical cut-off point (>14) for MELD-XI for predicting postoperative mortality among patients with heart failure undergoing left ventricular assist device (LVAD) implantation, and Yang et al (20) reported that a MELD-XI score of ≥17, which was close to our best cut-off value of 13.88, predicted long-term mortality after LVAD placement.

Our subgroup analyses also showed that the MELD-XI score was significantly higher among the deceased patients than the survived ones in the subgroup of patients presented with decompensated heart failure. This suggest that, as previous studies pointed (10,16,19,20,22,24), MELD-XI score is more related to decompensation of heart failure and thus venous congestion and resulting hepatic and renal dysfunction.

This finding was also corroborated by a higher MELD-XI score in the deceased patients within the CRT-D subgroup, which more commonly presented with decompensated heart failure than the ICD subgroup, which more commonly presented with device shock/electrical storm. These findings may suggest that MELD-XI score is a surrogate marker for renal and hepatic derangement, principally due to congestion, venous hypertension, and possibly low cardiac output. To the contrary, device shocks and electrical storm, when not accompanied/cause by congestion or low cardiac output, may not disturb hepatic hepatic and renal functions as severely as decompensated heart failure. As such, in patients with implanted devices device shocks and electrical storm may occur due to causes other than decompensated heart failure such as electrolyte imbalance, cardiac ischemia, infections, or drug proarrhythmia, although a notable proportion of patients may also present with decompensated heart failure causing device shocks. However, as the majority of device shock/electrical storm cases (72.2%; 13 out of 18 cases) in our study were not secondary to decompensated heart failure but other conditions such as stable monomorphic ventricular tachycardia, ischemia, infections, electrolyte disorders, and COPD exacerbations, and as there occurred only one death in the appropriate shock/electrical storm subgroup, we could not assess whether MELD-XI score affected mortality rate in the appropriate shock/electrical storm subgroup.

Our study has several limitations. First, it had a retrospective design. Second, only patients with ICD or CRT-D were included and patients with conventional pacemakers were excluded. This was because patients with a history of heart failure and low left ventricular ejection fraction requiring device therapy were included, who also frequently admit with decompensated heart failure and/or device shocks. Third, MELD-XI score only incorporates serum total bilirubin and creatinine, and does not include other confounding factors that affect mortality rate in decompensated heart failure and/or device therapy. Fourth, there occurred only one death in the appropriate shock/electrical storm subgroup, which prevented any assessment of the role of MELD-XI score on survival in this patient subgroup.

CONCLUSION

MELD-XI score predicted in-hospital mortality among patients with ICD or CRT-D admitted to coronary care unit with decompensated heart failure or device shock/electrical storm. MELD-XII score appears especially useful among decompensated heart failure patients presenting with electrical storm, as those carrying a CRT-D who also more commonly presented with decompensated heart failure. These data suggest that MELD-XII score successfully predicts in-hospital mortality by reflecting heart failure decompensation through impaired renal and hepatic function.
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