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Clinical paper

RAPID-ED: A predictive model for risk assessment of patient's early in-hospital deterioration from emergency department

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Abstract

Introduction: The objective of this multi-center retrospective cohort study was to devise a predictive tool known as RAPID-ED. This model identifies non-traumatic adult patients at significant risk for cardiac arrest within 48 hours post-admission from the emergency department.

Methods: Data from 224,413 patients admitted through the emergency department (2016–2020) was analyzed, incorporating vital signs, lab tests, and administered therapies. A multivariable regression model was devised to anticipate early cardiac arrest. The efficacy of the RAPID-ED model was evaluated against traditional scoring systems like National Early Warning Score (NEWS) and Modified Early Warning Score (MEWS) and its predictive ability was gauged via the area under the receiver operating characteristic curve (AUC) in both hold-out validation set and external validation set.

Results: RAPID-ED outperformed traditional models in predicting cardiac arrest with an AUC of 0.819 in the hold-out validation set and 0.807 in the external validation set. In this critical care update, RAPID-ED offers an innovative approach to assessing patient risk, aiding emergency physicians in post-discharge care decisions from the emergency department. High-risk score patients ($\geq$13) may benefit from early ICU admission for intensive monitoring.

Conclusion: As we progress with advancements in critical care, tools like RAPID-ED will prove instrumental in refining care strategies for critically ill patients, fostering an improved prognosis and potentially mitigating mortality rates.

Keywords: Predictive model, Emergency medicine, In-hospital mortality, ICU, Mechanical ventilation

Introduction

Patient safety and quality improvement are critical concerns in healthcare, especially in the Emergency Department (ED). Prompt recognition of clinical deterioration remains a significant challenge for emergency physicians. Despite ED checkpoints, rapid patient deterioration upon moving to the general ward persists. Identifying at-risk patients during ED stays is crucial for reducing morbidity and mortality. Proposed solutions include extended monitoring in observation units, timely interventions, and systematic use of scoring systems to identify high-risk patients.[1,2]

Scoring systems aid physicians in evaluating and stratifying patient risks, yet widely used ones like Acute Physiology and Chronic Health Evaluation,[3,4] Simplified Acute Physiology Score,[5,6] Laboratory-based Acute Physiology Score,[7] and Comorbidity Point Score,[8] initially designed for ICU patients, may not effectively predict early deterioration in those initially admitted to the general ward,[9] introducing bias in non-critical patient assessments. Specific tools like Rapid Emergency Medicine Score focus on ED patients' total in-hospital mortality risk,[10] while Mortality in Emergency Department Sepsis score caters to populations like sepsis patients.[11] Triage in Emergency Department Early Warning Score relied on the initial vital signs upon ED arrival for predicting in-hospital mortality, rather than incorporating the serial vital signs, laboratory tests, or other measurements throughout the patient's ED stay.[9] Despite these systems, there is currently no scoring system available that can accurately predict early deterioration for patients admitted to the general ward from the ED.

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https://doi.org/10.1016/j.resplu.2024.100570
Received 27 November 2023; Received in revised form 15 January 2024; Accepted 25 January 2024

In this study, we aim to develop a predictive model called RAPID-ED (Risk Assessment of Patient's Early In-hospital Deterioration from Emergency Department) that can identify high-risk patients who are likely to experience early mortality following hospital admission from the ED. The primary goal of the study is to develop a predictive model provides emergency physicians with the information they need to make more informed clinical decisions, leading to improved patient outcomes and reduced morbidity and mortality rates.

Materials and methods

Study setting and patient population

The study methodology is presented in Fig. 1. This retrospective study utilized the Electronic Health Record from three medical centers in northern, central, and southern Taiwan to identify patients at high risk for early CA following ED admission. The study period was from January 1, 2016, to December 31, 2020, and included non-traumatic patients aged > 20 years old who were admitted to hospital wards via the ED. Patients who were admitted directly to the ICU from the ED, discharged against medical advice, or transferred to other hospitals during admission were excluded.

Data collection

Variables associated with the patients' medical history, vital signs, laboratory tests, and ED management were collected. Vital signs at ED triage and upon discharge to the ward were both collected to better reflect the patient's condition change during ED observation. The patient's shock index, calculated as heart rate divided by systolic blood pressure, was considered a useful monitor index that associates with the patient's clinical status was also collected.[10] Additionally, management details, both pharmacological and non-pharmacological, including emergency physician decisions like Do-Not-Resuscitate (DNR) orders, were considered variables in the analysis.

The database provided a large amount of data that was valuable for analyzing and improving patient-centered outcomes. However, it also presented the issue of missing values. In this study, we employed two strategies combining clinician's perspective and statistical approach to impute missing values, based on the missing rate for each variable.

For variables where missing values exceed 50%, we employ the median value within the reference range for imputation. Missing values for tests such as lipase, bilirubin, albumin, troponin, and blood pH are addressed in this manner. For instance, if a patient lacks lipase data, it may be because the clinician deemed the test unnecessary due to an anticipated normal result. Consequently, we impute it with a value of 38 u/l. By using the mean to fill in these missing values, our aim is to minimize potential bias in the analysis caused by missing data.

For the rest of the included variables, in which missing values rate under 50%, we used MissForest methods to fill in the blanks. MissForest is a method for imputing missing values in a dataset using a random forest model. MissForest creates multiple classification or regression trees and averages their predictions to fill in the

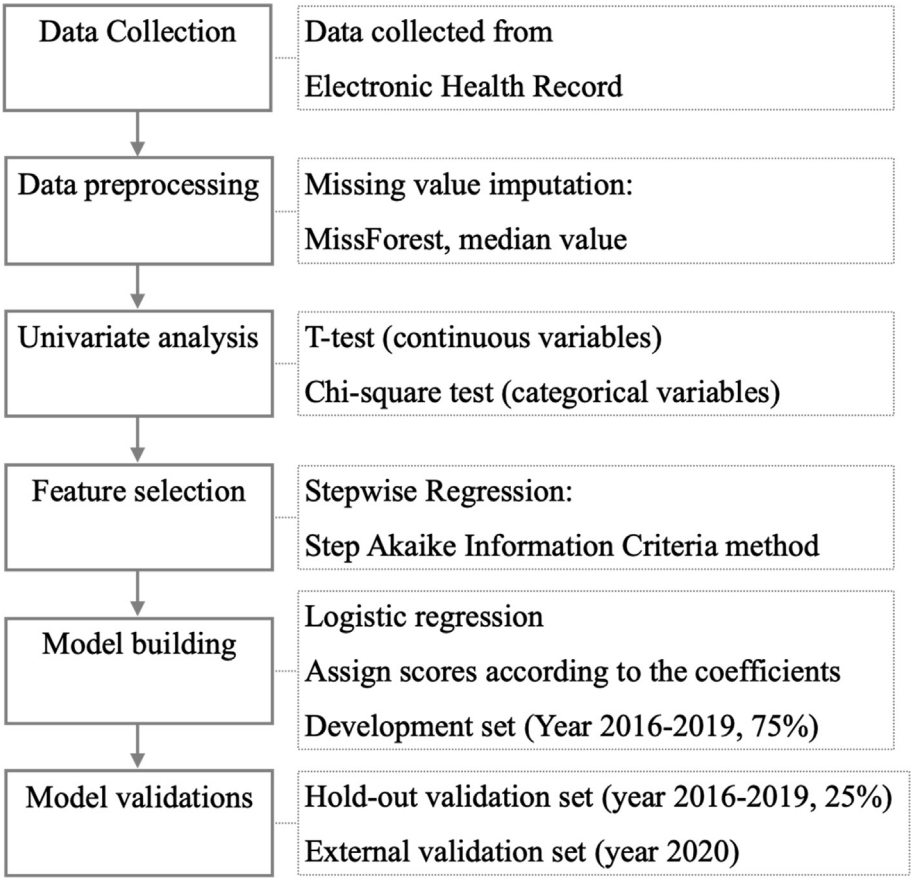

Fig. 1 – The development of RAPID-ED model.

missing values. It has been shown to outperform other imputation methods in comparative studies and has a good record of accuracy when estimating the error of its imputations.[11]

Outcome measurements

In this study, cardiac arrest (CA) occurring within 48 hours after hospital admission from ED was regarded as the target outcome.

Feature selection

In this study, we utilized stepwise regression with the Step Akaike Information Criteria (StepAIC) method for feature selection. The goal of StepAIC is to identify a parsimonious set of features that simplifies the model without compromising its performance. To achieve this, we sought to minimize the StepAIC value and iteratively remove features that did not contribute significantly to the model.[12]

The StepAIC provides a measure of the relative quality of statistical models, taking into account both the goodness of fit and the complexity of the model. By adopting StepAIC in our feature selection process, we aimed to identify a robust set of predictors for our predictive model that could effectively discriminate between patients at high and low risk of early in-hospital CA.

Development and validation of the predictive model

After identifying key predictors through stepwise regression, this study employed multivariable logistic regression to craft the RAPID-ED model for in-hospital CA. Assigning scores based on logistic regression model coefficients facilitated the creation of a concise risk stratification system. Coefficients were estimated in log odds, and each factor's point value was determined by dividing 0.2 by its coefficient and rounding to the nearest value. The value of 0.2 was chosen as the dividing factor for each variable's coefficient to determine its point value. This decision was based on considering 0.2 as an appropriate unit that effectively reflects the importance of each variable. Alternatively, it can be explained as the smallest even number when compared to the highest coefficient, which is 1.4. These coefficients can be used to calculate a risk score for each patient based on the values of their predictors. The higher the risk score, the higher the probability of experiencing an adverse event. The coefficients of the model provide a measure of the contribution of each predictor to the outcome risk estimation. The resulting model allows for the interpretation of each variable in terms of their marginal effect on the outcome.

To test the model's robustness through a rigorous process, we validated the model under two conditions: one with a randomly hold-out validation set, and the other with validation over a different time span compared to the development set. These were designated as the "hold-out validation set" and the "external validation set," respectively. The development set and hold-out validation set were chosen based on index dates before December 31, 2019, whereas the external validation set included patients from 2020, featuring index dates after that cutoff. All datasets were sourced from the same three medical centers. The development set and hold-out validation set were randomly split with a ratio of 3:1. The development set was used to develop the predictive model, while the hold-out validation set was used to assess the model's performance. Finally, the external validation set was used to evaluate the model's generalizability through time. By using different datasets for model development and validation, we aimed to reduce the risk of overfitting and to ensure that the predictive model could be applied to new patients and settings.

Statistical analysis

The Mann–Whitney U test and chi-square analysis were used to determine the variables that were correlated with in-hospital adverse events. Statistical significance was defined as a two-sided P-value less than 0.05.

To evaluate the performance of the predictive model, we compared it with traditional early warning scores, including the National Early Warning Score (NEWS) and Modified Early Warning Score (MEWS) in the hold-out and external validation dataset. The predictive performance of the models was assessed using the area under the receiver operating characteristic curve (AUROC). The corresponding sensitivity, specificity, and accuracy were calculated using the Youden Index, and the 95% confidence interval (CI) was calculated using the Clopper–Pearson method.

All statistical analyses were conducted using the R studio 4.0.3 version for Mac. To ensure the validity and reliability of our results, we followed rigorous statistical procedures and conducted sensitivity analyses to assess the robustness of our findings. Our statistical approach enabled us to identify significant predictors of in-hospital adverse events and assess the performance of our predictive model compared to traditional scores. The study adheres to The Strengthening the Reporting of Observational Studies in Epidemiology Statement for reporting purposes.[13]

Results

The patient inclusion process is outlined in Fig. 2, with 224,413 patients included in the model development and validation from the original 1,150,546 enrolled participants. Supplementary Table 1 presents the basic demographic and clinical characteristics of the development, hold-out validation, and external validation groups. The demographic characteristics, past medical history, vital signs, laboratory studies, and treatments received during ED were comparable between the development and hold-out validation sets. Statistically significant differences between the development and external validation sets may be attributed to the different data collection periods.

Analysis of patient characteristics

Table 1 summarizes the findings from the development set's univariate analysis, comparing patients who experienced CA within 48 hours of in-hospital admission to those who did not. Key differences include higher mean age (70.9 vs. 66.9 years, $p < 0.0001$), increased prevalence of elderly (age > 65 years, 65.9% vs. 56.6%, $p = 0.001$) and extreme elderly patients (age > 80 years, 30.5% vs. 23.0%, $p = 0.002$), elevated physiological markers (pulse 102.8 vs. 95.8 bpm, $p < 0.0001$, 21.4 vs. 19.8 breaths/min, $p < 0.0001$), higher incidence of shock index > 1 (21.9% vs. 10.6%, $p < 0.0001$), Glasgow Coma Scale (GCS) < 12 (32.5% vs. 13.0%, $p < 0.0001$), and GCS < 8 (15.2% vs. 4.9%, $p < 0.0001$) in the CA group. Therapeutic limitations, indicated by DNR orders, were more common in the CA group (32.5% vs. 4.2%, $p < 0.0001$). Lab results showed higher levels of various markers in the CA group, including blood sugar, total bilirubin, aspartate aminotransferase, creatinine, potassium, C-Reactive Protein (CRP), white blood count, segment, and band form. The CA group also had a higher prevalence of comorbidities such as coronary artery disease (17.9% vs. 13.3%, $p = 0.02$), heart failure (18.5% vs. 12.2%, $p = 0.0007$), malignancy (44.4% vs. 28.4%, $p < 0.0001$), and end-stage renal disease (27.5% vs. 22.8%, $p < 0.0001$). During the ED period, the CA group received oxygen

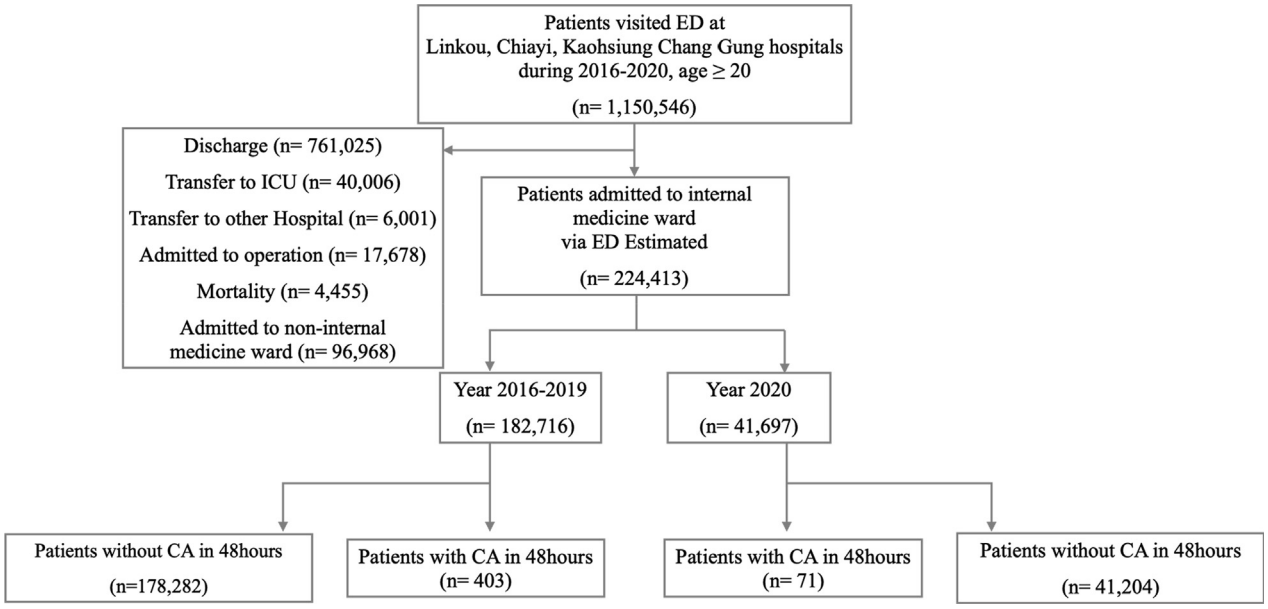

Fig. 2 – Patient inclusion flow chart.

Table 1 – Baseline characteristics of CA and no CA group. Numeric variables are presented as mean (standard deviation). Categorical variables are presented as numbers (percentages).

Variable	CA n = 302	No CA n = 136,735	P value
Age	70.9(14.9)	66.9(16.3)	<0.0001
Age > 65	199(65.9%)	77446(56.6%)	0.001
Age > 80	92(30.5%)	31496(23%)	0.002
Gender			0.43
Male	180(59.6%)	78429(57.4%)	
Female	122(40.4%)	58306(42.6%)	
Sign [1]DNR	98(32.5%)	5803(4.2%)	<0.0001
Vital Sign			
[2]TMP [3](a) (°C)	36.9(1.2)	36.9(1.1)	0.85
PULSE(a) (bpm)	102.8(24.9)	95.8(21.6)	<0.0001
[4]SBP(a) (mmHg)	128.7(34.5)	139.2(32.2)	<0.0001
[5]DBP(a) (mmHg)	75.2(20.2)	80.4(17.6)	<0.0001
[6]RR(a) (breaths/min)	21.4(4.6)	19.8(3.2)	<0.0001
Shock index(a)	0.9(0.3)	0.7(0.3)	<0.0001
[7]SI(a) > 1	66(21.9%)	14451(10.6%)	<0.0001
GCS sum(a)	10.6(3.6)	12.1(2.2)	<0.0001
GCS(a) < 12	98(32.5%)	17734(13%)	<0.0001
GCS(a) < 8	46(15.2%)	6641(4.9%)	<0.0001
TMP [8](d) (°C)	36.5(0.9)	36.5(0.7)	0.29
Pulse(d) (bpm)	99.1(20.6)	84.2(16.8)	<0.0001
SBP(d) (mmHg)	125(24)	131.6(23.9)	<0.0001
DBP(d) (mmHg)	72(16.5)	76.4(14.5)	<0.0001
RR(d)	21.3(5.9)	18.3(2.5)	<0.0001
Shock index(d)	0.7(0.2)	0.8(0.2)	<0.0001
SI(d) > 1	44(14.6%)	4498(3.3%)	<0.0001
GCS_sum(d)	55.7(110.3)	73(124.9)	0.006
GCS(d) < 12	103(34.1%)	19177(14%)	<0.0001
GCS(d) < 8	65(21.5%)	4758(3.5%)	<0.0001
Laboratory Test			
Sugar(mmol/L)	175.6(86.3)	159.1(83.1)	0.001
Lipase(U/L)	52.1(197.3)	52.3(254.4)	0.99
Direct.Bilirubin(mg/dl)	0.5(1.8)	0.3(1)	0.08
Total.Bilirubin (mg/dl)	2.1(4.4)	1.2(2.2)	0.0003

Table 1 (continued)

Variable	CA n = 302	No CA n = 136,735	P value
AST	67(187.7)	37.7(168.6)	0.007
ALT	49.3(121.7)	41.2(143.1)	0.25
Creatinine(mg/dL)	2.2(2.1)	1.8(2.2)	0.0001
Sodium(mmol/L)	133.5(7.8)	135.4(5.2)	<0.0001
K(mmol/L)	4.2(0.8)	3.9(0.6)	<0.0001
[9]CRP(mg/L)	105.6(92.3)	62.9(66.3)	<0.0001
Albumin(g/dL)	4(0.6)	4.2(0.4)	<0.0001
Troponin I(ng/ml)	0.2(0.9)	0.1(1.7)	0.2
Segment	80(13.6)	74.6(13.5)	<0.0001
Band	1.6(4.8)	0.4(1.9)	<0.0001
WBC (10^4/L)	13.3(9)	10.5(9.2)	<0.0001
Hb (g/dl)	10.7(2.4)	11.6(2.5)	<0.0001
platelet (10^9/L)	210.4(116.3)	217.1(103.7)	0.32
Pco2(mmHg)	37.8(6.7)	38(3.3)	0.61
pH	7.4(0.04)	7.4(0.03)	0.6
Hco3(mmol/L)	22.8(3.3)	23(1.9)	0.19
Past History			
Diabetes mellitus	104(34.4%)	43552(31.9%)	0.34
Liver Cirrhosis	34(11.3%)	14984(11%)	0.87
Coronary Artery Disease	54(17.9%)	18159(13.3%)	0.02
Heart Failure	56(18.5%)	16651(12.2%)	0.0007
Cerebrovascular accident	47(15.6%)	23822(17.4%)	0.4
Malignancy	134(44.4%)	38823(28.4%)	<0.0001
End stage renal disease	83(27.5%)	31199(22.8%)	0.05
Hypertension	126(41.7%)	59842(43.8%)	0.47
ED measurement			
[10]Low O2	211(70%)	50115(36.7%)	<0.0001
[11]High O2	71(23.5%)	3447(2.5%)	<0.0001
Vasopressor	17(5.6%)	2247(1.6%)	<0.0001
Fluid Challenge	95(31.5%)	17756(13%)	<0.0001

[1]DNR, Do-Not-Resuscitate; [2]TMP, body temperature; [3](a), (ED arrival); [4]SBP, systolic blood pressure; [5]DBP, diastolic blood pressure; [6]RR, respiratory rate; [7]SI, shock index; [8](d), (ED discharge); [9]CRP, C-reactive protein; [10]Low O2, oxygen therapy < 50% or < 10L; [11]High O2, oxygen therapy ≥ 50% or ≥ 10L.

therapy (70.0% vs. 36.7%, p < 0.0001), inotropic vasopressor support (5.6% vs. 1.6%, p < 0.0001), and fluid resuscitation (31.5% vs. 13.0%, p < 0.0001) more frequently than the non-CA group.

Feature selection and development of predictive model

To identify significant risk factors for CA within 48 hours of ED discharge, we performed univariate analysis using variables with p < 0.001. The stepwise regression method was used to determine the most influential predictors for CA. The selected variables, their ranges, and points comprising the scores are presented in Table 2. The total score for predicting CA risk was calculated by summing the point value of each predictor variable, which included pulse rate, respiratory rate, GCS, total bilirubin, CRP, segment, malignancy, DNR, and oxygen therapy. The final risk score ranged from 0 to 39, with a higher score indicating a higher risk of CA. For physiological variables, the value before ED discharge was considered.

Evaluation of model performance

In terms of the primary outcome, the RAPID-ED model generated AUC values of 0.819 (95% CI, 0.797–0.841) and 0.807 (95% CI, 0.782–0.831) in the hold-out and external validation sets, respectively, for predicting CA. The scoring system could be applied with different cutoff points to balance model sensitivity and specificity, as illustrated in Supplementary Table 2. Based on a score of 10 as the optimal cutoff point, the model achieved a balance between sensitivity (71.3%) and specificity (79.2%) for predictive CA.

Table 2 – The RAPID-ED scores. The calculated value is obtained by summing the assigned point value of each predictor variable.

Predictor	Score
Pulse ≥ 100 bpm	4
Respiratory Rate ≥ 35 breaths/min	6
GCS < 8	5
Total Bilirubin ≥ 2 mg/dl	5
CRP	
40–80 mg/L	2
>80 mg/L	3
Segment	
75–85%	2
>85%	3
Malignancy	2
DNR	4
O2	
Low flow < 50% or < 10L	4
High flow ≥ 50% or ≥ 10L	7

Fig. 3 shows a comparison of the developed model with traditional early warning scores. RAPID-ED exhibited superior predictive performance in anticipating CA compared to both NEWS (AUC[95% CI]: 0.761[0.737–0.784]) and MEWS (AUC[95% CI]: 0.770[0.749–0.795]) during hold-out validation (AUC[95% CI] = 0.819[0.797–0.8

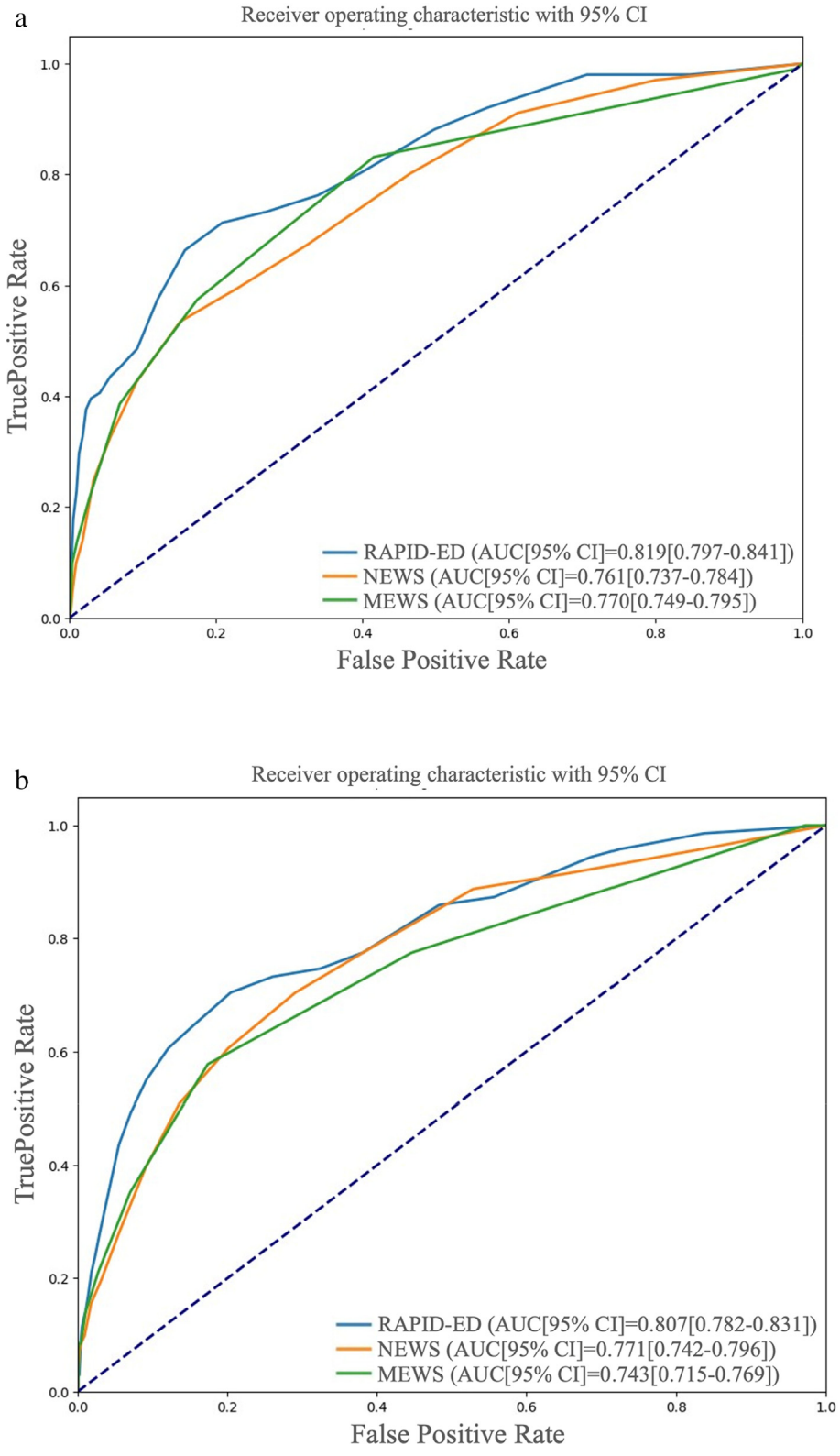

Fig. 3 – (a) Comparative assessment of predictive models and traditional early warning scores through AUROC analysis in hold-out validation set. (b) Comparative assessment of predictive models and traditional early warning scores through AUROC analysis in external validation set.

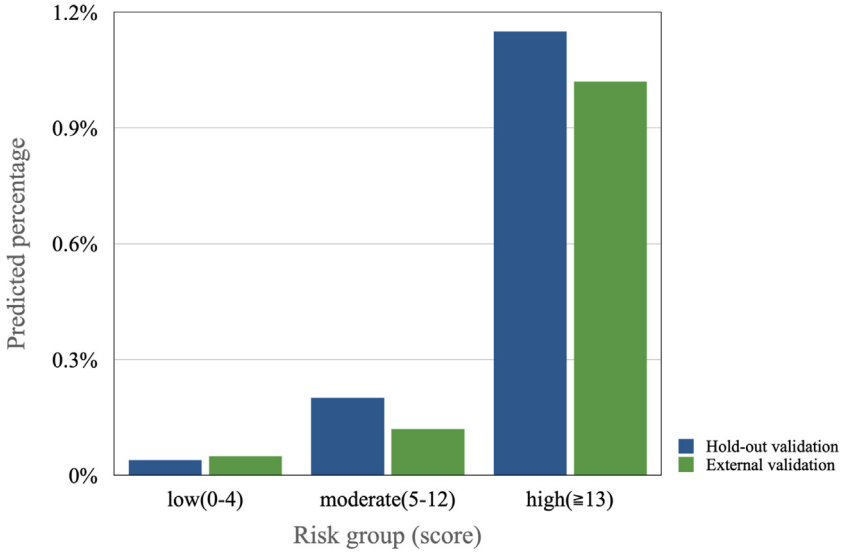

Fig. 4 – The result of risk stratification in hold-out validation set and external validation set.

41]). In external validation (AUC[95% CI] = 0.807[0.782–0.831]), while there was no significant difference from NEWS (AUC[95% CI] = 0.771[0.742–0.796]), RAPID-ED outperformed MEWS (AUC [95% CI] = 0.743[0.715–0.769]).

Fig. 4 presents the predicted risk of CA according to RAPID-ED. The study cohort was divided into three groups based on the score cutoffs: low risk (score, 0–4), medium risk (score, 5–12), and high risk (score $\geq$ 13). Patients in the high-risk group had a higher incidence of CA. In the hold-out validation, patients classified as high-risk group experienced an early CA occurrence of 1.15%, signifying a sixfold increase compared to those in the moderate-risk group (0.2%) and a twentyfold rise compared to individuals in the low-risk group (0.04%). Similar trends were noted in the external validation group, with early CA rates of 0.05% for the low-risk group, 0.12% for the medium-risk group, and 1.02% for the high-risk group.

Discussion

This study aimed to develop and validate an early mortality prediction model, RAPID-ED, for patients admitted to the hospital through the ED within 48 hours. This multivariable regression model showed improved performance in stratifying high-risk patients compared to previous early warning scoring systems. To account for the potential impact of data generation period on the model's performance, we divided our data collection into hold-out validation (2016–2019) and external validation (2020). To simulate the use of the predictive algorithm in real-world dynamic environments, we isolated patients with index dates in 2020 for external validation. Fig. 3 indicates that the multivariable regression model's performance was similar in both hold-out and external validation, suggesting that the model is unaffected by data sample variance. Thus, it can accurately predict early mortality consistently over time.

The model's score is a valuable tool for emergency physicians deciding ICU admission post-ED. We categorized patients into risk groups (Fig. 4). For example, in the external validation dataset with 3,475 ED patients admitted to the internal medicine ward each month, there were 6 cases of CAs. Applying the RAPID-ED model to this dataset could successfully identify 3 high-risk patients, aiding physicians in making decisions for early ICU admission to ensure close monitoring and care.

The performance of early mortality scoring systems may vary depending on the patient population being assessed. While scores designed to predict critical events are useful, their narrow selection of variables can limit their sensitivity to patient risk in other domains of acuity.[14] MEWS is designed to identify patients at risk of experiencing cardiac or pulmonary arrest, with limited capacity in capturing more subtle changes.[15–17] A study revealed lower accuracy of NEWS in predicting mortality for non-ICU patients with infections. Additionally, NEWS showed inadequate sensitivity in the elderly population.[18–21] Fortunately, our multivariable regression model enhances risk stratification for ED patients at risk of early mortality upon general ward admission, surpassing NEWS and MEWS in predicting early critical events.

In our model, pulse rate and respiratory rate are vital for early mortality detection. Studies indicate abnormal vital signs precede 85% of patient deteriorations, suggesting preventability in many negative outcomes.[22] In addition, GCS score is a well-calibrated model that has been widely used to predict long-term survivors.[23,24] In our multivariable regression model, CRP emerged as a significant predictor of early CA, aligning with findings from other studies. For instance, various reports note pre-existing sepsis rates in patients experiencing in-hospital CA, ranging from 13% to 27%.[25] Additionally, high CRP levels at ICU admission correlate with increased organ dysfunction, prolonged stays, and higher mortality.[26]

Studies seek to predict clinical deterioration in patients with hematologic malignancies, who face heightened risks in critical illness due to their complex medical needs.[27,28] A history of malignancy contributes to the risk of early detection in our study. We included patients with DNR orders, emphasizing the importance of discussing potential outcomes with the patient as part of managing critically ill individuals.[16,29,30] RAPID helps identify critically ill patients for DNR discussions, aligning with the patient's care goals. RAPID-ED evaluates the patient's oxygen therapy instead of relying on pulse oximetry, avoiding uncertainties in determining oxygen saturation levels, especially with the patient on room air.[31]

Limitations

This study had several limitations. First, this study in Taiwan may not apply directly to other ethnic groups. Yet, we conducted multi-center studies across various Taiwanese cities for external validation and to mitigate selection bias. Second, due to missing records, patients' original physiological characteristics (height, body weight, BMI) and personal habits (smoking, alcohol consumption) were not considered. In this regard, we collected patients' laboratory data and clinical conditions as much as possible. Third, other prehospital risk-scoring systems may require further investigation for comparison. Nevertheless, our results suggest strong tool integrity, indicating potential broad application in future clinical decision-making.

Conclusions

In this study, we developed RAPID-ED, a predictive model for assessing in-hospital CA after ED admission. Our model performed well in predicting early mortality, utilizing a simple scoring system with physiological variables, lab studies, and clinical information. It outperformed traditional scores, such as NEWS and MEWS, in predicting CA. Identifying high-risk patients (RAPID-ED score $\geq$ 13) enabled prompt management and improved disposition, potentially enhancing outcomes. RAPID-ED holds promise as a valuable tool for identifying high-risk patients, enabling close monitoring and early intervention for improved outcomes and efficient resource allocation in the ED.

Funding

This study was supported in part by research grants from the Kaohsiung Chang Gung Memorial Hospital (CMRP-G8M0231).

CRediT authorship contribution statement

Yi-Min Wang: Writing – review & editing, Writing – original draft. **I-Min Chiu:** Writing – review & editing, Writing – original draft. **Yu-Ping Chuang:** Software, Methodology, Data curation. **Chi-Yung Cheng:** Resources, Project administration, Methodology. **Chun-Fu Lin:** Writing – review & editing, Writing – original draft. **Fu-Jen Cheng:** Visualization, Validation, Supervision. **Chien-Fu Lin:** Writing – original draft, Writing – review & editing. **Chao-Jui Li:** Visualization, Validation, Resources, Project administration.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.resplu.2024.100570.

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