Original Article

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External Validation of the TERMINAL-24 Score in Predicting Mortality in Patients with Multiple Trauma

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Abstract:

Objective: A prediction model: "TERMINAL-24," was developed and internally validated for use in predicting the early mortality of multiple trauma patients in the Emergency Department. In this study, this model's external validity and generalizability was evaluated.

Material and Methods: A retrospective cohort was used for the construction of two datasets. Temporal external validation used the dataset from the same location at a different period, and geographic external validation used the dataset from a different location.

Results: In total, 1,932 patients underwent temporal external validation, with 14 (0.7%) patients dying within 8 hours, 35 (1.8%) patients died between 8 and 24 hours, and 1,883(97.5%) patients were alive at 24 hours. From this, 2,336 patients were eligible for geographical external validation, with 106 (4.5%) patients having died at the emergency room, 143 (6.1%) patients died in hospital and 2,087 (89.3%) patients survived. The TERMINAL-24 score was applied to both

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datasets, with a benchmark of 4 or higher (range 0-5). In the temporal dataset, this score showed a mortality of greater than 20% (specificity 0.97) area under the receiver operating characteristic curve (AuROC) 0.91 (95% confidence interval (CI) 0.85-0.96); whereas, it demonstrated a mortality of greater than 60% (specificity 0.99) AuROC 0.92 (95%CI 0.89-0.94) in the geographical dataset.

Conclusion: TERMINAL-24 was effective at predicting early death in the emergency room. It was successfully implemented within the same hospital; however, the cut-point should be adapted for application in other institutions with unspecified times of death. Prospective studies at different hospitals should be planned to generalize this scoring system for clinical practice.

Keywords: early mortality, multiple trauma, prognostic factor**,** validation

Introduction

The TERMINAL-24 (Traumatic Emergency Room Major INjury death At Least 24 hours) scoring system, with a total score of 0-5, is based on 4 components: hypotension, tachycardia, Glasgow Coma Scale (GCS) <9, and traffic injury; was developed previously (Clinical Prediction Scoring Scheme for 24 Hour Mortality in Major Traumatic Adult Patients)[1]. This scoring focuses on early deaths; between 8 and 24 hours, and particularly within 8 hours, which is the time frame targeted for patient resuscitation in an emergency room. The score utilizes simple and practical factors to predict the likelihood of mortality, with no requirement of laboratory or radiologic results making it beneficial to any emergency setting. It is also applicable to identify patients in the high-risk category when they arrive at an emergency department (ED) with limited resources, as it allows for a rapid referral to the trauma center. Additionally, this score could help the trauma center prioritize the most critical patients for an emergency intervention; specifically those with a high risk of death within 8 hours. This scoring system can also be applied to other situations where there is overcrowding in the emergency room; such as prioritizing trauma patients for admission to either the Intensive Care Unit (ICU) or the general ward.

It has been demonstrated that the TERMINAL-24 score was pragmatic via internal bootstrapping validation in the prior setting; a tertiary care hospital with a 24-hour presence of an emergency physician, no trauma team on duty, but a general surgeon being available to assist and perform operations, with all necessary resources; including a blood bank, a laboratory and a radiologic department being available. Although the score was validated in such a setting, it was not fully appropriate for use without external validation. Therefore, the effectiveness of the TERMINAL-24 score in other settings must be demonstrated before applying to general practice, because emergency departments may have different settings; for example, the physician on duty might be a general practitioner in community hospitals or emergency physicians in tertiary hospitals. Additionally, the availability of trauma teams, limited materials and resources to manage trauma patients; such as the operating room, radiology and laboratory may differ.

This study aimed to evaluate the accuracy of the TERMINAL-24 score, using a new data set; referred to: 'as external validation.' Using data from the same setting, but at different time periods, known as temporal validation, and data from different settings; known as geographical validation. These can be achieved by choosing another tertiary care hospital, which may have different rates of death and outcome definitions for testing generalizability.

Material and Methods

This study was comprised of 2 external validation datasets; these being: temporal and geographical validation.

Temporal external validation was performed by using the same setting over a different period. It included injured patients, over 15 years of age that had been classified as an emergency or resuscitation level receiving treatment at Nakornping Hospital; from January 2018 to December 2019. The previous study constructed the score from the collected data from January 2012 to December 2017.

Geographical external validation was tested using the data from another tertiary care hospital, Ayutthaya Hospital, which has approximately 15,000 trauma patients transiting through the emergency room, and a mortality rate of 6.0% per year. The data included injured patients above the age of 15, who were classified as an emergency or resuscitation level, from January 2012 and December 2017.

Study populations were defined similarly to the previous study[1]. In brief, this included patients above 15 years of age that were triaged as an emergency and critically sick to the emergency room for resuscitation, using the emergency severity index (ESI) system[2]. The data from the hospital's injury database (IS data: Injury Surveillance system) were extracted. All data were classified into demographic profiles (gender, age), prehospital profiles (Blunt or penetrating injuries, traffic/ assault or falling injury, and transferred by referral or by an emergency response team), and hemodynamic profiles (blood pressure, pulse rate, respiratory rate at triage area, and level of consciousness using the Glasgow coma scale). Data pertinent to patients who had had sudden cardiac arrest before being admitted to the emergency room were eliminated. The TERMINAL-24 score of each patient was generated using this formula: TERMINAL-24 score=1* hypotension (SBP<90) +1* tachycardia (HR≥120) +2*coma (Glasgow coma scale<9) +1* traffic injury, total score: 0-5. Three parameters were determined as the first patient arrived at the emergency department.

The main outcome was to determine the order of death within the first 24 hours. In the temporal dataset, early death was defined as death within 8 hours, and between 8 and 24 hours. Due to the data collection the geographical -Station, TX, USA). Each patient's TERMINAL-24 score was calculated, and the average of the score was presented using the median/interquartile range (IQR) for each group of death. The difference in score and distribution across levels is shown by a distributive box plot. The Hosmer-Lemeshow test was used to calibrate the goodness-of-fit of the model. The performance of the score was determined by the sensitivity, specificity and mortality rate. The AuROC curve was used for the prediction of mortality.

The characteristics of predictors between the development and validation groups were then compared. The TERMINAL-24 scores from each development and validation dataset were used to predict death in less than 24 hours, and are displayed as a receiver operating characteristic curve (ROC) combination between the two groups. Finally, a prediction curve was created, by combining the data from the development and validation groups to examine the mortality patterns of each TERMINAL-24 score. From this the suitability of the scores for clinical decision making in the emergency room was summarized.

Results

In total, 1,932 patients fitted the inclusion criteria for temporal external validation, with 0.7% as death within 8 hours, 1.8% deaths between 8 and 24 hours, and 97.5% patients alive after 24 hours. A total of 2,336 patients were eligible for geographical external validation: 4.5% deaths in the emergency room, 6.1% deaths in the hospital, and 89.3% survivors. All subjects in the external validation data were enrolled (Supplement Figure 1). As indicated in the study flow, there were 3,149 participants in the development group and 4,268 in the validation group for comparison, with score development data and external validation data (Figure 1). For each mortality sequence, the baseline characteristics and predictors for all patients used for external validation were different; particularly for all variables used in calculating the TERMINAL-24 score: as shown in Table 1.

The median/IQR of the groups of death within 8 hours, between 8-24 hours, and alive at 24 hours were 3(3-4), 3(2-4) and 1(0-1), respectively, for the temporal dataset. For the geographical dataset, the median/IQR of death in the emergency room, death in the hospital, and survived until discharged were 3(2-4), 3(1-3) and 1(0-1), respectively. As demonstrated in the distribution box plot, each score of the death and alive groups differed (Figure 2A, 2B). Death within 8 hours could be separated from between 8 and 24 hours on a score scale of larger than 4 in the Temporal dataset and Geographical dataset when using the TERMINAL-24 score. Based on the intersection of probability curves, a score greater than 3 can distinguish between death within 24 hours and death over 24 hours (Figure 2C, 2D).

The Hosmer-Lemeshow goodness-of-fit-test in the temporal dataset was 0.109 and 0.721 for mortality before 8 hours and between 8 and 24 hours, respectively. It was supposed to help predict mortality between 8 to 24 hours. In the geographical dataset, a value of 0.001 was found to be the same for predicting death in emergency rooms and hospitals, leading to the assumption that the results were inaccurate. (0.1 means not accurate and close to 1 means very accurate). Therefore, a table was created showing the sensitivity, specificity and mortality rate of each score, so as to assess the accuracy of the scores. (Table 2) When considering the cut point of the score for clinical decision-making; Table 2 shows the TERMINAL-24 score of both validation groups. In the temporal validation, a score of more than 3 exhibited a mortality rate of 9.0%; with a specificity of 0.96, indicating that patients were suited for admission to the ICU, and a score of more than 4 indicates a potential mortality rate of 22.7%, with a specificity of 0.96; indicating that a surgeon needs to be called to the emergency room immediately. In the geographical validation, it was discovered that a score of more than 2 demonstrated a mortality rate of 20.4%, with a specificity of 0.94; indicating that these patients should be admitted to the ICU. Moreover, a score of more than 3 indicated a mortality rate of 54.5%, with a specificity of 0.99; indicating that the surgeon should be notified to standby in the emergency room.

In both development and validation datasets (temporal and geographical external validation), the characteristics of factors used to generate the TERMINAL-24 score were significantly different: as shown in Table 3. When the ROC curve was generated, using development data, temporal external validation data and geographical external validation data for each order of death, it was discovered that the temporal validation dataset had a better predictive accuracy of death under 24 hours than the development dataset (AuROC; 0.83 (95% CI 0.77-0.90) and 0.66 (95% confidence interval (CI) 0.63-0.71), respectively). (Figure 3A) When comparing the geographical and temporal validation groups to the development group, the prediction accuracy of fewer than 8 hours of death was higher in the geographical and temporal validation groups (AuROC; 0.92 (95% CI 0.89-0.94), 0.91 (95% CI 0.85-0.96), and 0.74 (95% CI 0.66-0.82), respectively). (Figure 3B) For both development and validation datasets, there was an inflection point at the score over 3 for predicting death within 24 hours (Figure 3C). However, for predicting death under 8 hours, a score exceeding 2 in the geographical external validation showed a higher probability of death; unlike the development and temporal external validation dataset with a turning point of 3 or higher (Figure 3D).

Discussion

The TERMINAL-24 scoring system[1] is a system for calculating scores to predict mortality in severely injured people, with an emphasis on death within 8 hours, between 8 and 24 hours, and being alive at 24 hours. In a previous study[1], the comparison to previous trauma scores; i.e., Revised Trauma Score (RTS)[3,4], Injury Severity Score (ISS)[5], and Glasgow Coma Scale, Age, and Systolic Blood Pressure (GAP) score, revealed that TERMINAL-24 had promising accuracy. The accuracy in predicting mortality, determined by the AuROC, values of RTS, ISS and GAP were 0.59, 0.58, and 0.83, respectively, while the TERMINAL-24 score predicted mortality, with the area under ROC curve of 0.70. The cut point of above 4 from the TERMINAL-24 score could predict mortality rate at 16.1% with a specificity of 0.98, risk estimation validity of 84.7%, and a likelihood ratio of positive (LHR+) of 8.7 (95%CI; 4-13.5). Importantly, the TERMINAL-24 score was demonstrated to be beneficial for decision-making by identifying the risk of death. A score of more than 3 was chosen as a benchmark to admit the injured patients to an intensive care unit (ICU), or to activate the trauma team; including a surgeon for an immediate response at the emergency room. Internal validation of the TERMINAL-24 score, using the bootstrapping method, proved less overfit and revealed optimism for accuracy for early death prediction.

Table 1 Characteristics of patients with major trauma, for temporal and geographical external validation

Patient characteristics		Temporal external validation				Geographical external validation			
		Death <8 h n=14 (n, %)	Death 8-24 h n=35 (n, %)	Alive at 24 h n=1883 (n, %)	p-value	Death at ER n=106 (n, %)	In hospital Death n=143 (n, %)	Alive until discharge n=2087 (n, %)	p-value
Demographics	Male	11(78.6)	23(65.7)	1,428(75.8)	0.509	86(81.1)	104(72.7)	1,463(70.1)	0.016
	Age≥50	7(50.0)	20(57.1)	696(37.0)	0.023	39(36.8)	67(46.9)	648(31.1)	0.004
Vital signs	SBP<90*	9(64.3)	12(34.3)	126(6.7)	<0.001	26(24.5)	10(7.0)	62(3.0)	<0.001
	DBP<60	8(57.1)	17(48.6)	341(18.1)	<0.001	33(31.1)	20(14.0)	143(6.9)	<0.001
	PR≥120*	2(14.3)	8(22.9)	218(11.6)	0.134	34(32.1)	21(14.7)	203(9.7)	<0.001
	Abnormal RR (<10,>30)	13(92.9)	26(74.3)	349(18.5)	<0.001	83(78.3)	93(66.0)	191(9.2)	<0.001
Mechanism of injury	Traffic*	7(50.0)	21(60.0)	970(51.5)	0.618	87(82.1)	89(62.2)	1,270(60.9)	<0.001
	Fall	4(28.6)	8(22.9)	484(25.7)	0.894	9(8.5)	36(25.2)	416(20.0)	0.075
	Assault	2(14.3)	6(17.1)	247(13.1)	0.637	2(1.9)	3(2.1)	127(6.1)	0.013
	Other	1(7.1)	0(0.0)	182(9.7)	0.881				
Type of injury	Blunt	5(35.7)	16(45.7)	921(48.9)	0.598	12(11.3)	13(9.1)	177(8.5)	0.323
	Penetrating	0(0.0)	0(0.0)	84(4.5)	0.563	3(2.8)	1(0.7)	83(4.0)	0.147
	Combine	8(57.1)	12(34.3)	655(34.8)	0.225	14(13.2)	18(12.6)	58(2.8)	<0.001
	Other	1(7.1)	7(20.0)	223(11.8)	0.321	77(72.6)	111(77.6)	1,737(84.8)	<0.001
Glasgow coma scale	Mild (14-15)	1(7.1)	8(22.86)	1,460(77.5)	<0.001	1(0.9)	7(4.9)	1,835(88.0)	<0.001
	Moderate (9-13)	0(0.0)	1(2.9)	149(7.9)	0.535	19(18.0)	39(27.3)	1,29(6.2)	<0.001
	Severe* (3-8)	13(92.9)	26(74.3)	274(14.6)	<0.001	86(81.1)	97(67.8)	123(5.9)	<0.001
Transfer by	EMS	1(7)	5(14.3)	376(20.0)	0.418	63(59.4)	106(74.1)	1,052(50.4)	<0.001
	Refer	12(85.7)	30(85.7)	1,108(58.8)	<0.001	43(40.6)	37(25.9)	1,035(49.6)	<0.001
	Other	1(7.3)	0(0.0)	399(21.2)	0.470	-	-	-	-

Predictor to be calculated for TERMINAL-24 score=1 hypotension (SBP <90) +1* tachycardia (HR ≥120) +2*coma (Glasgow coma scale <9) +1* traffic injury
SBP=systolic blood pressure, DBP=diastolic blood pressure, PR=pulse rate, EMS=emergency medical service

Table 2 Temporal and geographical external validation of TERMINAL-24 scores, consisting of 3 groups of patients:death under 8 hours, death between 8-24 hours and alive at 24 hours (Temporal dataset); death in an emergency room, in-hospital death, and alive until discharge (geographical dataset). The sensitivity and specificity were calculated for the score in any group. The death rate is shown accompanying the TERMINAL-24 score

TERMINAL-24 score			0	1	2	3	4	5
Temporal external validation	Death under 8 hours	n	0	1	2	5	6	0
		sensitivity	1.00	0.93	0.79	0.43	0.00	0.00
		specificity	0.37	0.77	0.87	0.96	0.96	0.99
	Death between 8-24 hours	n	5	2	6	11	9	2
		sensitivity	0.86	0.80	0.63	0.31	0.06	0.00
		specificity	0.38	0.78	0.88	0.97	0.97	1.00
	Alive at 24 hours	n	710	761	192	161	51	8
	Death (%)		0.70	0.39	4.00	9.04	22.73	20.00
Geographical external validation	Death at Emergency room	n	0	9	18	48	25	6
		sensitivity	1.00	0.92	0.75	0.29	0.06	0.00
		specificity	0.35	0.87	0.94	0.99	0.99	1.00
	In hospital death	n	21	25	22	56	18	1
		sensitivity	0.85	0.68	0.52	0.13	0.01	0.00
		specificity	0.35	0.87	0.94	0.99	0.99	1.00
	Alive until discharge	n	722	1094	156	87	26	2
	Mortality (%)		2.83	3.01	20.41	54.45	62.32	77.78

Sensitivity and specificity range 0-1

Table 3 Discrimination performance of characteristic data of multiple trauma patients in the development group (n=3173): temporal validation group (n=1932), and geographical validation group (n=2336)

Characteristic	Development group n (%)	Temporal validation group n (%)	p-value	Geographical validation groupn (%)	p-value
Systolic blood pressure <90 mmHg	307 (9.8)	147 (7.6)	0.010	98 (4.2)	<0.001
Pulse rate ≥120 bpm	492 (15.6)	228 (11.8)	<0.001	25 (11)	<0.001
Glasgow coma scale <9	635 (20.1)	313 (16.2)	0.001	306 (13.1)	<0.001
Traffic injury	1531 (48.4)	998 (51.7)	0.009	1446 (61.9)	<0.001

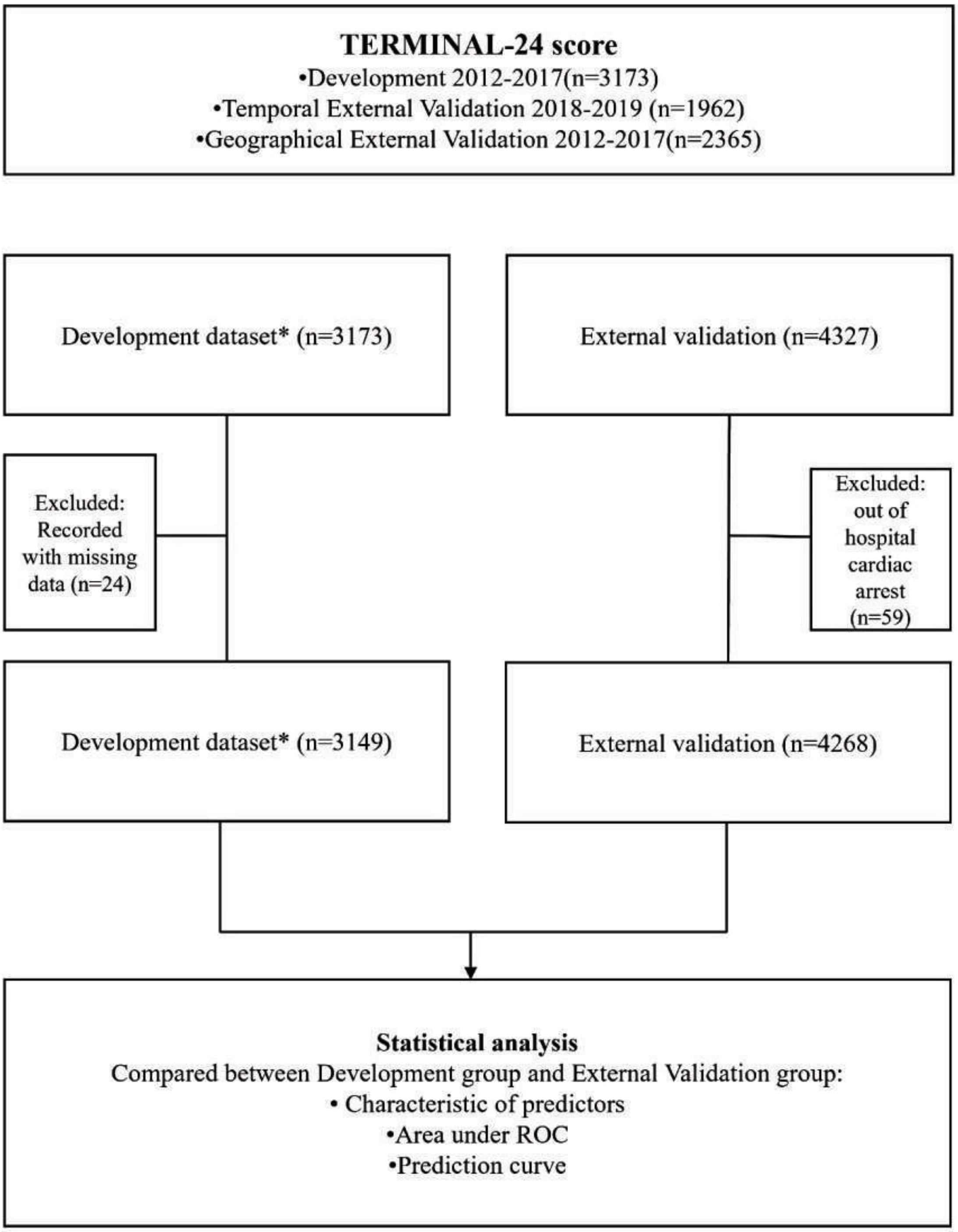
This scoring system focuses on predicting early death in trauma patients, and is based on the Advanced Trauma Life Support (ATLS) trimodal death[7]. In other words, the prevention of early death from injury should be focused on as those patients that should be prioritized in the emergency room. Despite prior research on the timing and causes of injury death, several studies[8-16] classified early death as death within 24 hours[8,9,14-16]. As a result, the TERMINAL-24 score is a more accurate scoring system for emergency room death prediction.

Although the emphasis of one of the scoring systems, GAP[6], was on death in the emergency room or operating room, it includes any injuries with an ISS score of 3 or higher, which is considered a minor injury according to the ISS definition[5] wherein, the TERMINAL-24 score focuses on the critically injured group, based on the ESI criteria of triage level 1-2[2]: this differs from GAP[6] inclusion criteria. Another scoring system, the EMTRAS[17] uses the same inclusion criteria as the TERMINAL-24 score; however, it focuses on hospital death, and is not appropriate for use in the emergency room.

The TERMINAL-24 score can be calculated immediately after the arrival of the patient at the emergency room, using their systolic blood pressure, pulse rate, Glasgow coma scale and traffic damage without the use of a calculator, which is essential for some scoring systems[3,4]. Additionally, the equation is also simple. Most notably, it does not require radiology or laboratory data, as does the ISS[5] or the EMTRAS[17], making it ideal for use in an emergency room; particularly for those with radiological and laboratory examination constraints. Although variables in scoring systems; such as REMS[18], MGAP[19], GAP[6] and NTS,[20] can be collected immediately in the emergency room there are multiple systolic blood pressure and pulse rate intersection points. This makes it difficult for the users, and the outcomes of these scores are either a prediction of 30-day mortality or death in hospital, which are not as appropriate for emergency room use.

When comparing the accuracy of the TERMINAL-24 score, by calculating the AuROC curve of the death sequence in the dataset of development (Nakornping Hospital, 2012-2017), temporal (Nakornping Hospital, 2018-2019) and geographical validation (Ayutthaya Hospital, 2012-2017), both validation datasets had high accuracy to predict death within 8 hours or equivalent death at the emergency room; with an AuROC curve of over 90.0%, compared to the development dataset, which had an AuROC curve of only 74.4%. (Figure 3B). This demonstrated that the TERMINAL24 score was accurate in predicting death in the emergency room. For the prediction of death within 24 hours, the TERMINAL-24 score performed well, with an accuracy of 83% in the temporal validation set, compared to an accuracy of 66.6% in the development dataset from Nakornping Hospital (Figure 3A). However, we could not compare it with the development data from Ayutthaya Hospital due to the unspecified time of death from this dataset.

The cut point of scores to be used in each emergency department can be determined using the sensitivity, specificity, and mortality rate of the TERMINAL-24 score (Table 2), the discrimination curve of TERMINAL-24 scores (Figures 2C and 2D) and the prediction curve of death at 8 and 24 hours (Figure 3C and 3D). In case of mass casualty, there is a concern n preventing an early death within 8 hours. Therefore, patients should be admitted to the ICU when their TERMINAL-24 score is greater than 3, and the surgeon should be contacted at the emergency room if the score is higher than 4 (Figures 2C and 3D). The score cut point should be determined by death rate, and it could be adjustable to the management of each hospital.



*Development dataset was from previous study[1]

Figure 1 Study flow of compared TERMINAL-24 score between the development and validation groups.

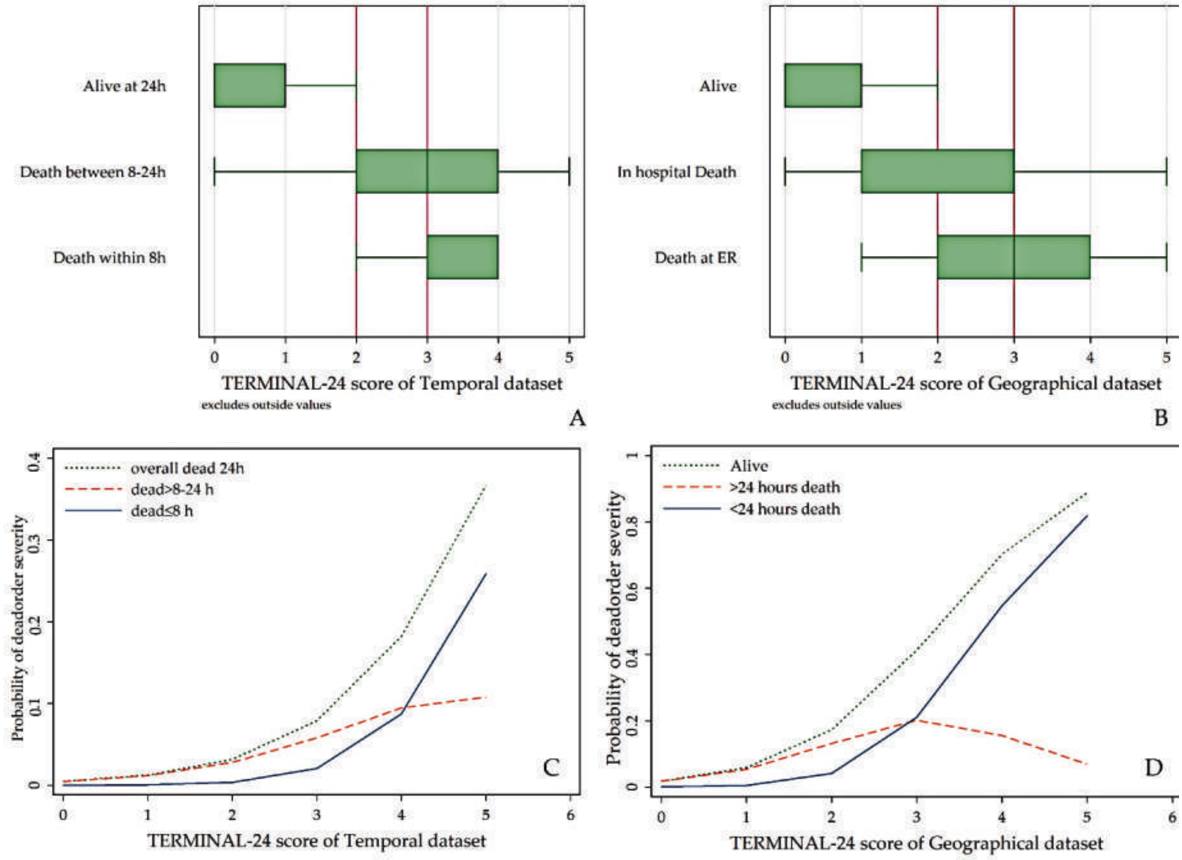


Figure 2 Distribution of TERMINAL-24 scores, and discrimination of death, based on TERMINAL-24 scores; 2A shows temporal external validation, 2B shows geographical external validation; by criterion-classified severity levels. (The vertical line in the box represents medians. Box boundaries represent 25th and 75th percentiles.) 2C shows Temporal external validation; a very short dashed line is the probability of overall death in 24 hours, a longer dashed line is the probability of death between 8-24 hours and the solid line is the probability of death under 8 hours and 2D: Geographical external validation; very short dash line is the probability of overall death, a longer dash line is the probability of death in the hospital and the solid line is the probability of death in an emergency room

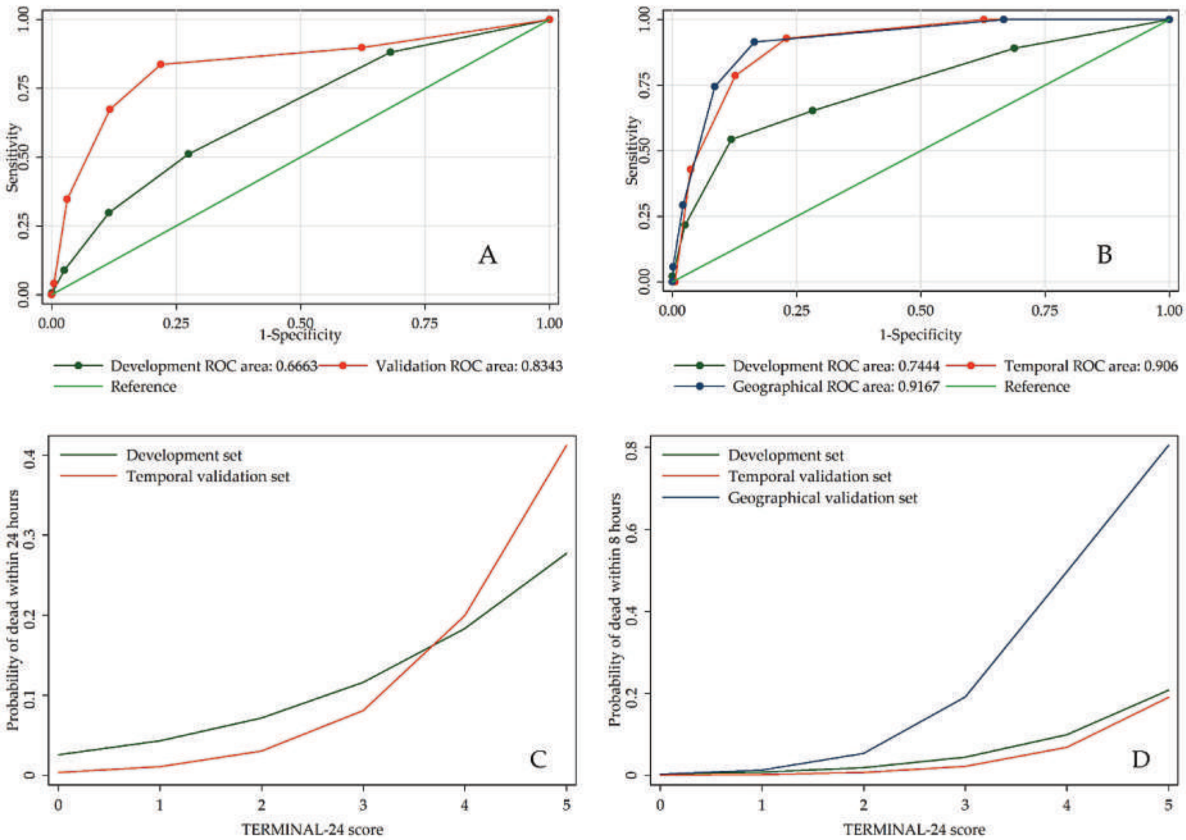


Figure 3 ROC curve combination of development and validation dataset and TERMINAL-24 score prediction curves. 3A: ROC curve combination of development and validation to predict death under 24 hours; 3B: ROC curve combination of development, temporal validation, and geographical validation to predict death under 8 hours. 3C: Prediction of death under 24 hours between development and temporal validation set; 3D: Prediction of death under 8 hours from development, temporal validation and geographical validation sets

In addition, according to the crosstab of different numbers, from the development dataset between death order and dead at the place (Supplementary Figure 2), the researcher plans to use the TERMINAL-24 score system in the emergency room care guidelines in the future. This would have an emphasis on early admittance to the intensive care unit in cases with a score=3 (mortality 11.0%), and early notification of the surgical team to evaluate trauma patients with an Emergency room score of 4 or above (mortality >16.0%).

Although the TERMINAL-24 scoring system was an acceptable tool for predicting the potential death of emergency room patients, when this scoring system was evaluated, using a different set of data to ensure its accuracy and validity, it was discovered that it was effective within the same hospital, However, there were limitations in terms of identifying the time of death, which cannot be described in hours and could only be specified as a death in the emergency department or death in the hospital for other hospitals. In a future study, prospective data from several hospitals should be obtained, with a focus on the precise time of mortality, so as to increase the sample size; particularly regarding death under 8 hours and death between 8 and 24 hours. Furthermore, this TERMINAL-24 score should be tested for user acceptability and the effectiveness in practice for multiple trauma patients.

Conclusion

TERMINAL-24 was effective at predicting early death in the emergency room. It was successfully implemented within the same hospital,; however, the cut-point should be adapted for application in other institutions with unspecified time of death. Prospective studies at different hospitals should be planned to generalize this scoring system for clinical practice.

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Conflict of interest

The authors declare no conflicts of interest.

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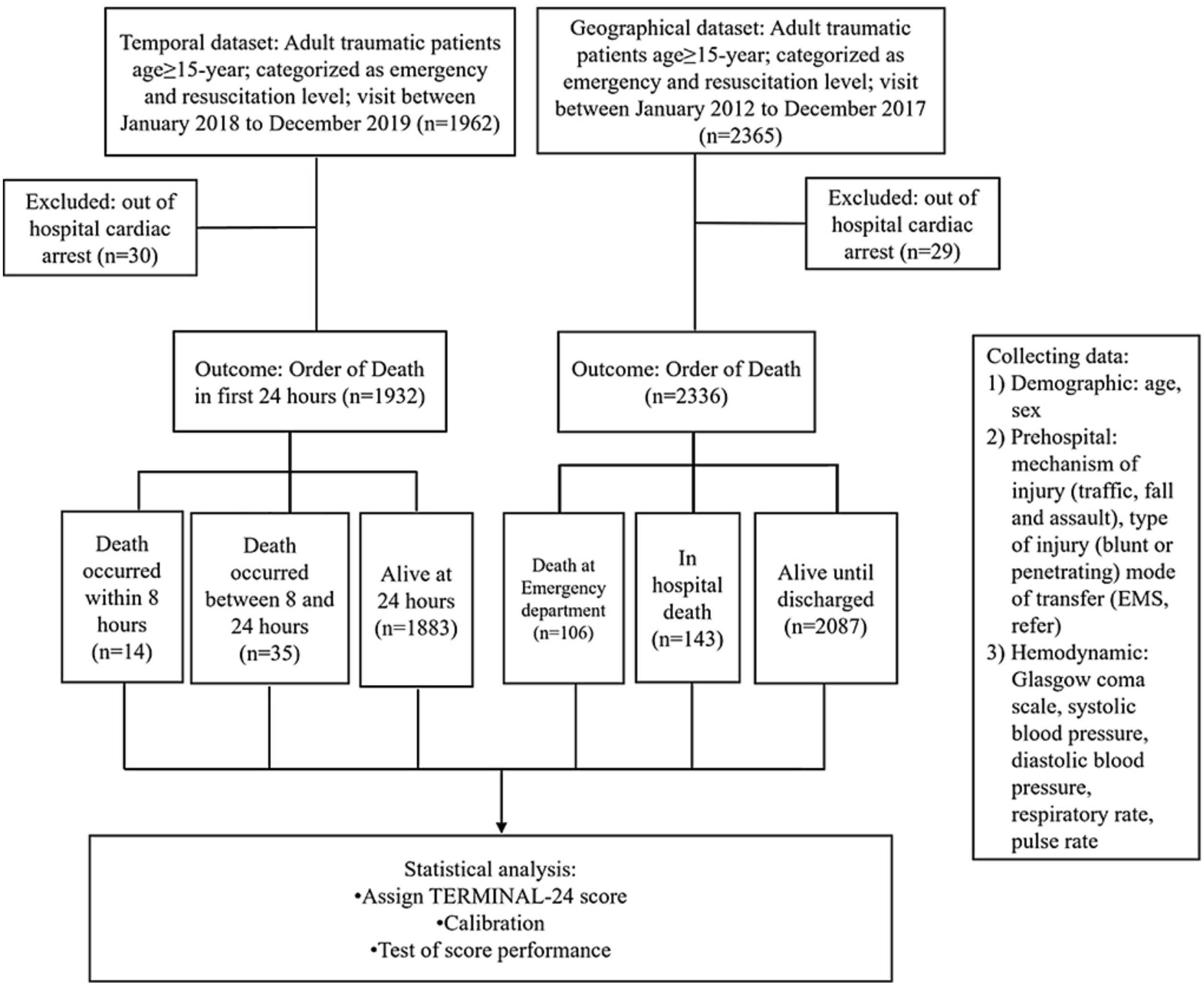
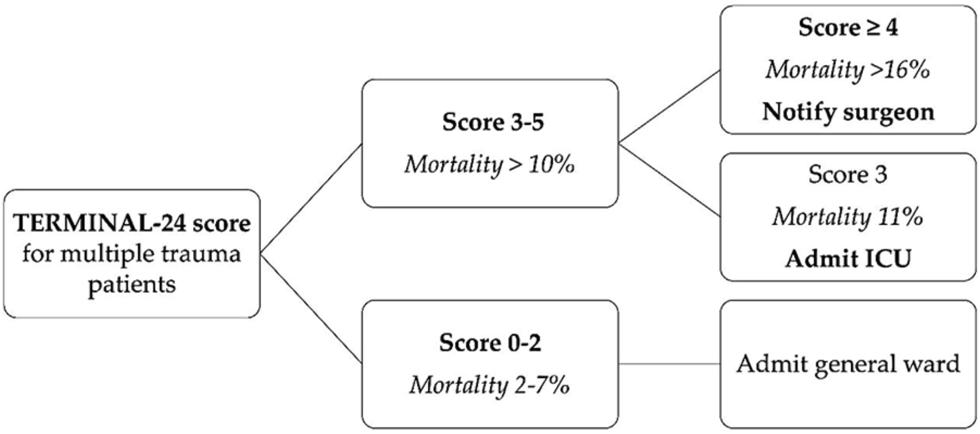


Supplementary Figure 1 Study flow of external validation dataset



Supplementary Figure 2 Future guideline for multiple trauma patients