Prediction of Mortality in a Patient With Acute Poisoning

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Research

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Abstract

Objective: This study aimed to develop a scoring system for predicting the in-hospital mortality of acute poisoning patients at the emergency department (ED).

Methods: This was a retrospective analysis of the Injury Surveillance Cohort generated by the Korea Center for Disease Control and Prevention (KCDC) from 2011–2018. We developed the new-Poisoning Mortality Scoring system (new-PMS) to generate a prediction model using the derivation group (2011–2017 KCDC cohort). Points were computed for each category of each variable. The sum of these points was the new-PMS. The validation group (2018 KCDC cohort) was subjected to external temporal validation. The performance of new-PMS in predicting mortality was evaluated using receiver operating characteristic (ROC) curves for both groups. For simple interpretation in clinical settings, risk groups were categorized as very low, low, intermediate, and high according to the new-PMS; we suggested the mortality curve according to new-PMS.

Results: Of 57326 poisoning cases, 42568 were selected. Of these, 34352 (80.7%) and 8216 (19.3%) were enrolled in the derivation and validation groups, respectively. New-PMS was the sum of points for each category of 10 predictors. The range of new-PMS was -20 to 3420 points. The area under the ROC curve of new-PMS was 0.942 (95% CI: 0.934–0.949) and 0.946 (95% CI: 0.930–0.963) for the derivation and validation groups, respectively. The mean predicted mortality and the observed mortalities of the high-risk group (new-PMS ≥1048) were 9.7% (95% CI: 9.3 – 10.0) and 10.0% for the derivation group and 8.4% (95% CI: 7.7 – 9.1) and 7.4% for the validation groups, respectively.

Conclusions: New-PMS showed good performance in predicting in-hospital mortality for both groups. As mortality sharply increased with the high risk-group of the new-PMS, early hemodynamic stabilization of acute poisoning patients at the ED may improve their clinical outcomes. New-PMS contributes to clinical decision-making for acute poisoning patients in clinical settings.

Background

Acute poisoning is a global health problem, and the prevention of mortality is essential in both intentional and accidental poisoning. The prediction of prognosis in acute poisoning patients has clinical significance for providing timely and appropriate treatment. However, toxicology research lacks a well-accepted method for assessing the severity of poisoning [1-3]. The Poisoning Severity Score (PSS), which has been used in toxicology as a disease-specific scoring system, is used infrequently and, when applied, has been misused or modified from its original form [4]. In its current form, it has limited clinical utility and likely cannot be broadly applied to many cases owing to their unique clinical circumstances [4].

Mortality prediction in acute poisoning has been explored with the application of the various clinical scoring systems used in critical care [5, 6]. The Acute Physiology and Chronic Health Evaluation (APACHE) score and the Simplified Acute Physiology Score (SAPS) are commonly applied tools in the intensive care unit; they are used for the prediction of outcomes in specific poisonings [7]. The mortality

of poisoning patients depends on not only their physiological condition but also the unique characteristics of the poisoning. The type of substance, route of exposure, and intent of poisoning affect the outcomes of acute poisoning patients. In addition, the toxic substance and its lethality are often unknown. A prediction model of mortality for acute poisoning patients has to consider both poisoning-related characteristics and the patient's physiological condition; moreover, it must be applicable to poisoning patients of all ages. The objective of this study was to develop a scoring system for predicting mortality in acute poisoning patients at the emergency department (ED). This work will assist in treatment allocation and therapeutic decision-making for acute poisoning patients at the early stages of poisoning.

Methods

Study design and selection of study patients

This study was a retrospective analysis of a prospective cohort from 23 EDs, namely the Injury Surveillance Cohort, which was generated by the Korea Center for Disease Control and Prevention (KCDC) from 2011 to 2018. This registry comprised prospectively collected data on the epidemiology and outcome variables of injury patients who presented at an ED [8]. The registry included poisoning cases as a type of injury. We selected poisoning patients from this cohort. This selected registry included the baseline characteristics of poisoning patients: age; sex; time-related factors, such as ED presenting time and poison exposure time; poisoning-related variables, such as the intent of poisoning, route of exposure, type of substance (7 categories and 44 types of substance); and initial vital signs at ED presentation, such as systolic blood pressure (SBP), heart rate (HR), respiration rate (RR), body temperature (BT), and AVPU scale of mental status. The registry also contained outcome-related variables, such as mortality at the ED or after hospital admission.

Patients who were transferred from the initial ED to another hospital; those who had incomplete data of poisoning-related variables, initial physiological condition-related variables, or outcome-related variables; and those who died on arrival at the ED were excluded from this study (Figure 1).

The selected study population was divided into two groups, namely the derivation group for the prediction of in-hospital mortality and the validation group for the external validation of the developed prediction model (Figure 1).

The Institutional Review Board of the Korea University hospital approved this study (IRB No. 2020AN0195).

Data analysis

The primary outcome was in-hospital mortality. We compared the characteristics of the poisoning patients between the derivation and validation groups (Table 1). Age, sex, time from exposure to ED presentation, classes of substance, intent of poisoning, route of exposure, vital signs of the patient at ED

presentation, and in-hospital mortality were analyzed (Table 1). For analysis, the variables related to poisoning characteristics were categorized as follows: intent of poisoning: 1) unintentional, 2) intentional, and 3) unknown; route of exposure: 1) dermal, ocular, or injection; 2) oral; and 3) inhalation; and toxic substance included 44 kinds of substances that were classified into eight categories from A to H. For categorization of substances, we considered the classification in the types of substances. And then we categorized the substances in the same classification according to the mortality index (MI) of each substance: A) pharmaceutical agents with MI of less than 0.5%, B) pharmaceutics with MI 0.5 – 5%, C) artificial toxic substances with MI of less than 1.0%, D) artificial toxic substances or pesticides with MI of 1.0 – 10.0%, respectively, E) artificial toxic substances or pesticides with MI of 11.0 – 20.0%, respectively, F) paraquat with MI of 52.5%, G) gases with MI of less than 1.0%, H) natural toxic substances with MI of less than 1.0% (Table 2)(An additional file 1 shows this in more detail [see Additional file 1]). The patient's physiological variables included age, SBP, HR, RR, BT, and mental status (AVPU scale), in accordance with the predictors in SAPS-II [9]. However, because SAPS-II does not include RR score, we categorized RR according to the normal range (12–24 breaths/min) [10, 11].

Development of the new poisoning mortality scoring system

We developed the new-Poisoning Mortality Scoring system (new-PMS) to generate a prediction model for the derivation group (2011–2017 data of the KCDC cohort) (Figure 1). First, we compared poisoning- and physiological condition-related variables between the patients who survived and were discharged (survivor subgroup) and those who died at the hospital (in-hospital death subgroup) among the derivation group (Table 3). We selected variables that had statistical and clinical significance in acute poisoning as predictors for developing the new-PMS [12]. Points for each category of each predictor were computed using multivariable logistic regression, in which the regression coefficient for each category of each predictor was converted into points by dividing the smallest regression coefficient in the model (Table 4) [13]. The sum of these points of each category in each predictor was the new-PMS.

Performance evaluation of the new-PMS

We analyzed the performance of the new-PMS in predicting mortality using receiver operating characteristic (ROC) curves in both the derivation and validation groups. The validation group (2018 data of the KCDC cohort) was subjected to external temporal validation.

For simple interpretation in a clinical setting, we created the following risk groups: very low, low, intermediate, and high risk according to the quartile range of the new-PMS. Real mortalities were investigated in the derivation and validation groups, respectively [12]. Moreover, we generated a mortality curve according to the new-PMS in the derivation group.

Statistical analysis

Continuous variables were reported as the median with interquartile ranges (IQR). Differences in the medians were compared using the Mann-Whiney U-test. Categorical variables were compared using the

chi-square test. All statistical analyses were performed using SPSS version 20.0 (IBMSPSS Inc., Chicago IL, USA). Two-tailed p values < 0.05 were considered statistically significant.

Results

Selection of the study population and outcomes

Of 57326 poisoning cases, 14758 (25.7%) were excluded: 3399 were transferred out of the ED, 239 had unknown outcomes, 10953 had incomplete data on poison-related variables, and 167 died on arrival at the ED (Figure 1). Of the 42568 included patients, 34352 (80.7%) and 8216 (19.3%) were enrolled in the derivation and validation groups, respectively (Figure 1). Among the study population, the median time from exposure to ED presentation was 2 h (interquartile range: 1.0–2.0 h). The incidence of in-hospital mortality was 909 (2.6%) and 135 (1.6%) for the derivation and validation groups, respectively (p < 0.001) (Table 1). The characteristics of the derivation and validation groups are presented in Table 1.

Development of the new-PMS in the derivation group

We compared characteristics between the survivor and in-hospital death subgroups in the derivation group (Table 2). The demographics, poisoning-related variables, and initial vital signs in each subgroup are shown in Table 2. Patients in the in-hospital death subgroup showed higher likelihood of older age, male sex, intentional poisoning, oral ingestion, and pesticide poisoning; they also initially presented with low SBP, high HR, high RR, and altered mental status compared with those in the survivor subgroup. Time from exposure to ED presentation was not significantly different between the survivor and in-hospital death subgroups (p = 0.057).

We selected 10 predictors from these variables considering clinical reasoning and statistical significance. The 10 predictors (age, sex, type of substance, intent of poisoning, route of poisoning, SBP, HR, RR, BT, and AVPU scale) and each category of each predictor are presented in Table 4. Multivariable logistic regression was used to calculate the points for each category of each predictor. First, we estimated the regression coefficient (B) for each category of each predictor in the multivariable logistic regression model. Next, the base constant B was selected as the smallest regression coefficient (B) in the model. The base constant B was 0.062 in the multivariable model (Table 4). We converted the regression coefficient (B) for each category of each predictor into points using the formula B/0.005 (Table 3) [13][13]. The points for each predictor were 0 to 480 for the age categories, 0 and 88 for the sex categories, 0 to 215 for the intent categories, 0 to 202 for the route categories, 0 to 1174 for the substance categories, -19 to 382 for the SBP categories, 0 to 195 for the HR categories, -1 to 140 for the RR categories, 0 and 133 for the BT categories, and 0 to 411 for the AVPU categories (Table 4). The new-PMS was the sum of the points of each predictor. The minimum to maximum range of the new-PSS was -20 to 3420 points.

Performance evaluation of the new-PMS

The performance of the new-PMS in predicting in-hospital mortality in acute poisoning was significantly high, with an area under the curve (AUC) of 0.942 (95% confidence interval [CI]: 0.934–0.949) in the derivation group ($p<0.001$) (Figure 2(A)). External temporal validation analysis of the new-PMS also showed a significantly high AUC of 0.946 (95% CI: 0.930–0.963) ($p < 0.001$) in the validation group (Figure 2(B)).

The median value of the new-PMS was 786 (inter quartile range: 593–1047) points in the derivation group. In risk-grouping for simple interpretation in clinical settings, patients were classified, according to the quartile range of the new-PMS, into four categories: ≤593 points, very low risk; 594–786 points, low risk; 787–1047 points, intermediate risk; and ≥1048, high risk (Table 5). The mean predicted mortality and the observed mortalities of the high-risk group (new-PMS ≥1048) were 9.7% (95% CI: 9.3 – 10.0) and 10.0% for the derivation group and 8.4% (95% CI: 7.7 – 9.1) and 7.4% for the validation groups, respectively (Table 5).

The mortality curve of the new-PMS showed an S-shape in the derivation group (Figure 3). In the new-PMS of 1048 points or above, the probability of in-hospital mortality increased very sharply (Figure 3).

Discussion

In this study, we developed the new-PMS to predict the probability of mortality in acute poisoning patients. The new-PMS is a simplified scoring system that is easy to use in clinical practice. The new-PMS comprises 10 predictors, including patient demographics, poisoning-related factors, and patient's initial vital signs.

Specific prediction outcome models in toxicology have limited value when applied to a wide range of poisoning patients. The PSS has been used in toxicology as a disease-specific scoring system [1]. It was developed in the 1990s in Europe to describe a patient's most severe symptomatology [1, 4]. However, the PSS has several subjective criteria, is time-consuming, and is likely to be of little use in some types of poisoning, limiting its clinical utility [4]. The development of a new poisoning severity scoring system is required for clinical use. The new-PMS developed in this study has several benefits, namely the use of objective predictors, the rapid assessment of mortality risk, and early applicability in clinical settings.

Several severity of illness models that have been used in the intensive care unit can be applied to acute poisoning patients. Silakhori [14] reported that the APACHE-II, APACHE-IV, SAPS-II, and SOFA have acceptable discriminatory power for poisoning patients, and APACHE-II can be used for mortality prediction in the early days of admission. However, this previous study included only 150 patients. When predicting the outcome of acute poisoning patients in clinical settings, we have to consider not only the physiological condition of the patient but also the unique characteristics of the poisoning. In the present study, 10 predictors were selected for the development of the new-PMS, considering toxicologic factors and the patient's physiological status. The predictors related to the patient's physiological status were categorized into age and vital signs, in accordance with SAPS-II [15], which has been commonly used to predict outcomes in poisoning patients. The new-PMS reflected the two major characteristics of acute

poisoning patients, namely the characteristics of the poisoning and of the early physiological condition after the poisoning.

Given the unique characteristics of individual xenobiotics, many researchers have attempted to apply physiological scoring systems in patients with specific xenobiotic poisoning [14-19]. However, outcome prediction models for specific toxic substances have a limitation of generalization. In the current study, the new-PMS showed excellent performance in predicting mortality, with an AUC of over 0.9 in all acute poisoning patients, regardless of the cause of poisoning, type of substance, age, and sex. The present study was an attempt to develop a new scoring system for outcome prediction in poisoning patients as an alternative to the PSS.

We used the multivariable logistic regression method to assign points for each category of each predictor. This method is commonly used for the development of prognosis prediction models [12, 13]. This approach has been used in numerous studies to create a risk scoring system [20, 21]. The reference category of each predictor was determined considering the lowest mortality or normal physiological variable value. For example, the mortality of the 40-year-old age group was 0.04%, which is the lowest among all age groups (Table 2).

The performance of the new-PMS was excellent according to the general guideline of the AUC in both the derivation and validation groups [22]. In simulation studies, the external validation of a prediction model requires a minimum of 100 events of the primary outcome, as a small external validation study is unreliable and inaccurate [23-25]. Our validation group had 135 mortality cases in a total of 8216 poisoning cases.

For easy use in clinical settings, we constructed the risk groups and a mortality curve of the new-PMS. The observed mortalities of the derivation and validation groups also increased according to the risk-grouping. We expect that the new-PMS may be useful for objective discrimination of the very-low-risk group at the poisoning call center and for allocating acute poisoning patients to poisoning treatment centers at the pre-hospital setting. Furthermore, the risk of mortality sharply increased in acute poisoning patients with the new-PMS of approximately 1048 points or above. These results suggested that early hemodynamic stabilization for high-risk poisoning patients at the ED may improve their clinical outcomes. The new-PMS will contribute to clinical decision-making and the therapeutic guidance of patients with acute poisoning.

Limitations

First, in this study, we excluded cases that had missing values of poisoning-, outcome-, and vital signs-related variables. The traditional ‘complete cases’ analysis may lead to selection bias of subjects and statistically inefficient results [12]. In addition, we excluded DOA patients from this study because we considered that these patients required no specific treatments for acute poisoning. Second, the amount of exposure in the cases of oral ingestion and the duration of exposure in the cases of inhalation or surface absorption are important for predicting the outcomes of acute poisoning patients. Unfortunately, our

cohort did not have data on the amount of exposure and the envenomation, such as animal bites. However, the new-PMS developed in this study included the unique characteristics of poisoning, such as the intent and route of poisoning. Third, we categorized the toxic substances into 8 categories comprising 44 specific substances, as all the 44 substances could not be inputted to the multivariable logistic regression. The clinical severity of a poisoning can range from asymptomatic to life-threatening, depending on specifics related to the toxin. For example, specific toxic substances, such as paraquat, are known to have high mortality by themselves without the consideration of other predictors [26]. In this study, we considered paraquat as a separated category. Further study with using machine learning method may improve the prediction of mortality with consideration of specific toxic substances. Lastly, the real observed mortalities in this study were as low as 2.6% for the derivation group and 1.6% for the validation group. There is a risk of overestimating/overfitting the predictive performance of the model if the number of predictors is much larger than the number of outcome events [12].

Conclusion

Because outcome prediction systems for poisoning patients are rarely studied, we developed a single scoring system to accurately predict outcomes in poisoning patients with a wide range of demographics. The new-PMS showed good performance in predicting the in-hospital mortality of acute poisoning patients, both in the derivation and validation groups. Because the risk of mortality sharply increased with the high risk-group of the new-PMS, early hemodynamic stabilization for acute poisoning patients at ED presentation may improve their clinical outcomes. The new-PMS will assist in clinical decision-making for patients with acute poisoning, thus improving their outcomes.

Declarations

Ethics approval and consent to participate

This study was approved by the Institutional Review Board of the Korea University hospital (#IRB No. 2020AN0195). This study was a retrospective study based on the de-identified administrative database, so the informed consents were waived.

Consent for publication

Not applicable

Availability of data and materials

The datasets during and/or analysed during the current study available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests. Neither the entire paper nor any part of its contents have been published or accepted by another journal. The paper has not been submitted in its entirety, or in part, to any other journal.

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Authors' contributions

KSH, SJK, and SWL conceived and designed the study and wrote the manuscript. KSH managed and analyzed the data, including data quality control. LJS provided advice on statistics. All authors contributed substantially to the writing of the manuscript.

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References

1. Persson HE, Sjöberg GK, Haines JA, Pronczuk de Garbino J: Poisoning severity score. Grading of acute poisoning. *Journal of toxicology Clinical toxicology* 1998, 36(3):205-213.
2. Lionte C, Sorodoc V, Jaba E, Botezat A: Development and validation of a risk-prediction nomogram for in-hospital mortality in adults poisoned with drugs and nonpharmaceutical agents: An observational study. *Medicine* 2017, 96(12):e6404.
3. Cheung R, Hoffman RS, Vlahov D, Manini AF: Prognostic Utility of Initial Lactate in Patients With Acute Drug Overdose: A Validation Cohort. *Annals of emergency medicine* 2018, 72(1):16-23.
4. Schwarz ES, Kopec KT, Wiegand TJ, Wax PM, Brent J: Should We Be Using the Poisoning Severity Score? *Journal of medical toxicology : official journal of the American College of Medical Toxicology* 2017, 13(2):135-145.

5. Alizadeh AM, Hassanian-Moghaddam H, Shadnia S, Zamani N, Mehrpour O: Simplified acute physiology score II/acute physiology and chronic health evaluation II and prediction of the mortality and later development of complications in poisoned patients admitted to intensive care unit. *Basic & clinical pharmacology & toxicology* 2014, 115(3):297-300.
6. Banderas-Bravo ME, Arias-Verdú MD, Macías-Guarasa I, Aguilar-Alonso E, Castillo-Lorente E, Pérez-Costillas L, Gutierrez-Rodriguez R, Quesada-García G, Rivera-Fernández R: Patients Admitted to Three Spanish Intensive Care Units for Poisoning: Type of Poisoning, Mortality, and Functioning of Prognostic Scores Commonly Used. *BioMed research international* 2017, 2017:5261264.
7. Bilgin TE, Camdeviren H, Yapici D, Doruk N, Altunkan AA, Altunkan Z, Oral U: The comparison of the efficacy of scoring systems in organophosphate poisoning. *Toxicology and industrial health* 2005, 21(7-8):141-146.
8. Korea Center for Disease Control & Prevention. Injury prevention for healthy & safe society. Available at: http://www.cdc.go.kr/contents.es?mid=a20602040000.
9. Le Gall JR, Lemeshow S, Saulnier F: A new Simplified Acute Physiology Score (SAPS II) based on a European/North American multicenter study. *Jama* 1993, 270(24):2957-2963.
10. Barrett KE, Barman SM, Brooks HL, Yuan JXJ. Ganong's Review of Medical Physiology. 26e. Section VI: Respiratory Physiology: Introduction. New York: McGraw-Hill;2012.
11. Flomenbaum NE, Goldfrank LR, Hoffman RS, Howland MA, Lewin NA, Nelson LS. Goldfrank's toxicolgic emergencies. 8th ed. New York: McGraw-Hill;2002. p40.
12. Han K, Song K, Choi BW: How to Develop, Validate, and Compare Clinical Prediction Models Involving Radiological Parameters: Study Design and Statistical Methods. *Korean journal of radiology* 2016, 17(3):339-350.
13. Sullivan LM, Massaro JM, D'Agostino RB, Sr.: Presentation of multivariate data for clinical use: The Framingham Study risk score functions. *Statistics in medicine* 2004, 23(10):1631-1660.
14. Silakhori S, Dadpour B, Khadem-Rezaiyan M, Sedaghat A, Mirzakhani F. Comparing APACHE II, APACHE IV, SAPS II, and SOFA Predictive Power in Poisoned Patients Admitted to the Intensive Care Unit. Int J Med Toxicol Forensic Med, 2020. 10(2).
15. Shadnia S, Darabi D, Pajoumand A, Salimi A, Abdollahi M: A simplified acute physiology score in the prediction of acute organophosphate poisoning outcome in an intensive care unit. *Human & experimental toxicology* 2007, 26(8):623-627.
16. Sheta AA, El-Banna AS, Elmeguid RA, Mohamed HE, Gad NH: A study of the predictive factors of mortality in acute poisoning with aluminum phosphide with special reference to echocardiography and SOFA score. *Environmental science and pollution research international* 2019, 26(32):33135-33145.
17. Cho YS, Moon JM, Chun BJ, Lee BK: Use of qSOFA Score in Predicting the Outcomes of Patients With Glyphosate Surfactant Herbicide Poisoning Immediately Upon Arrival at the Emergency Department. *Shock (Augusta, Ga)* 2019, 51(4):447-452.

18. Kaojarern S, Ongphiphadhanakul B: Predicting outcomes in paraquat poisonings. *Veterinary and human toxicology* 1991, 33(2):115-118.
19. Kim YH, Yeo JH, Kang MJ, Lee JH, Cho KW, Hwang S, Hong CK, Lee YH, Kim YW: Performance assessment of the SOFA, APACHE II scoring system, and SAPS II in intensive care unit organophosphate poisoned patients. *Journal of Korean medical science* 2013, 28(12):1822-1826.
20. Schnabel RB, Sullivan LM, Levy D, Pencina MJ, Massaro JM, D'Agostino RB, Sr., Newton-Cheh C, Yamamoto JF, Magnani JW, Tadros TM *et al*: Development of a risk score for atrial fibrillation (Framingham Heart Study): a community-based cohort study. *Lancet (London, England)* 2009, 373(9665):739-745.
21. Imperiale TF, Monahan PO, Stump TE, Glowinski EA, Ransohoff DF: Derivation and Validation of a Scoring System to Stratify Risk for Advanced Colorectal Neoplasia in Asymptomatic Adults: A Cross-sectional Study. *Annals of internal medicine* 2015, 163(5):339-346.
22. Muller MP, Tomlinson G, Marrie TJ, Tang P, McGeer A, Low DE, Detsky AS, Gold WL: Can routine laboratory tests discriminate between severe acute respiratory syndrome and other causes of community-acquired pneumonia? *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America* 2005, 40(8):1079-1086.
23. Collins GS, Ogundimu EO, Altman DG: Sample size considerations for the external validation of a multivariable prognostic model: a resampling study. *Statistics in medicine* 2016, 35(2):214-226.
24. Vergouwe Y, Steyerberg EW, Eijkemans MJ, Habbema JD: Substantial effective sample sizes were required for external validation studies of predictive logistic regression models. *Journal of clinical epidemiology* 2005, 58(5):475-483.
25. Collins GS, de Groot JA, Dutton S, Omar O, Shanyinde M, Tajar A, Voysey M, Wharton R, Yu LM, Moons KG *et al*: External validation of multivariable prediction models: a systematic review of methodological conduct and reporting. *BMC medical research methodology* 2014, 14:40.
26. Min YG, Ahn JH, Chan YC, Ng SH, Tse ML, Lau FL, Chan CK: Prediction of prognosis in acute paraquat poisoning using severity scoring system in emergency department. *Clinical toxicology (Philadelphia, Pa)* 2011, 49(9):840-845.

Tables

Table 1. Comparison of patient characteristics between the derivation and validation groups

	Derivation group (n = 34,352)	Validation group (n = 8,216)	p value
Patient characteristics	14432 (42.0)	3573 (43.5)	<0.001
Age (years)	11961 (34.8)	2698 (32.8)	
< 40, n (%)	3288 (9.6)	842 (10.2)	
40–59, n (%)	1592 (4.6)	275 (3.3)	
60–69, n (%)	1515 (4.4)	364 (4.4)	
70–74, n (%)	1564 (4.6)	464 (5.6)	
75–79, n (%)			
≥ 80, n (%)			
Sex	15514(45.2) : 18838(54.8)	3579(43.6) : 4637(56.4)	0.009
Male : female (%)			
Poisoning-related factors	2 (1–5)	2 (1–5)	0.931
Time from exposure to presentation (h)	12738 (37.1)	2769 (33.7)	<0.001
	21158 (61.6)	5421 (66.0)	<0.001
Intent of poisoning	456 (1.3)	26 (0.3)	<0.001
Unintentional, n (%)	346 (1.0)	4 (0.5)	
Intentional, n (%)	27531 (80.1)	6443 (78.4)	
Unknown, n (%)	6475 (18.8)	1769 (21.1)	
Route of poisoning	16449 (47.9)	4484 (54.6)	
Dermal, ocular, or injection, n (%)	5461 (15.9)	893 (14.1)	
Oral ingestion, n (%)	6160 (17.9)	1666 (20.3)	
Inhalation, n (%)	4876 (14.2)	879 (10.7)	
Classification of substances	1406 (4.1)	294 (3.6)	
Pharmaceutics, n (%)			
Pesticides, (%)			
Gases, n (%)			
Artificial toxic substances, n (%)			
Natural toxic substances, n (%)			
Initial vital signs at Emergency Department	30239 (88.0)	7264 (88.4)	0.081

Systolic Blood Pressure (mmHg)	279 (0.8)	85 (1.0)	<0.001
100 – 199, n (%)	3577 (10.4)	815 (9.9)	<0.001
≥ 200, n (%)	257 (0.7)	52 (0.6)	0.885
70 – 99, n (%)	27185 (79.1)	6383 (77.7)	<0.001
≤ 69, n (%)	4032 (11.7)	1086 (13.2)	
Heart Rate (beat/min.)	2974 (8.7)	724 (8.8)	
70 – 119, n (%)	161 (0.5)	23 (0.3)	
30 – 69, n (%)	31940 (93.0)	7825 (95.2)	
120 – 159, n (%)	76 (0.2)	10 (0.1)	
≥ 160, n (%)	2336 (6.8)	381 (4.6)	
Respiration Rate (breath/min.)	34276 (99.8)	8199 (99.8)	
12 – 24, n (%)	76 (0.2)	17 (0.2)	
≤ 11, n (%)	24448 (71.2)	5517 (67.1)	
≥ 25, n (%)	5668 (16.5)	1628 (19.8)	
Body Temperature (℃)	3646 (10.6)	931 (11.3)	
< 39, n (%)	590 (1.7)	140 (1.7)	
≥ 39, n (%)			
Mental status, n (%)			
Alert			
Verbal response			
Pain response			
Unresponse			
Outcome	909 (2.6)	135 (1.6)	<0.001
In-hospital mortality, n (%)			

Table 2. Category of exposed of substances according to the class of the substance and the mortality index in the derivation group

Category	Name of substance		
A	1) hormones, hormone antagonists, contraceptions	2) agents for diagnosis	3) vitamin, dietary supplements
	4) topical preparations	5) acetaminophen	6) antipsychotics
	7) antidepressant	8) zolpidem	9) doxylamine
	10) unspecified sedatives, antipsychotics, hypnotics	11) benzodiazepine	
B	1) peptic, gastrointestinal drugs	2) antihistamine	3) cold and cough preparation
	4) unspecified therapeutic drugs	5) anticonvulsants	6) cardiovascular drugs
	7) unspecified analgesics	8) antibiotics, antifungals	9) opioid
	10) stimulants, street drugs	11) asthma therapies	12) oral hypoglycemic drugs
C	1) alcohols (liquor, ethanol, methanol)	2) heavy metals	3) hydrocarbons
	4) chlorine bleach, sodium hypochlorite		
D	1) unspecified artificial toxic substances	2) unspecified alkali	3) unspecified acid
	4) unspecified corrosive agents	6) unspecified insecticides	7) pyrethroid
	5) rodenticide	9) unspecified herbicides	10) glyphosate
	8) unspecified pesticides		
E	1) glacial acetic acid	2) organophosphate	3) carbamate
F	1) paraquat		
G	1) carbon monoxide	2) unspecified gases	
H	1) natural toxic substances		

Table 3. Comparison of characteristics between the survivor and in-hospital death subgroups in the derivation group

	Survivor (n = 33,443)	In-hospital death (n = 909)	p value
Patient characteristics	14373 (43.0)	59 (6.5)	<0.001
Age (years)	11732 (35.1)	229 (25.2)	
< 40, n (%)	3139 (9.4)	149 (16.4)	
40–59, n (%)	1438 (4.3)	154 (16.9)	
60–69, n (%)	1374 (4.1)	141 (15.5)	
70–74, n (%)	1387 (4.1)	177 (19.5)	
75–79, n (%)			
≥ 80, n (%)			
Sex Male : female (%)	14892(44.5) : 18551(55.5)	622(68.4) : 287(31.6)	<0.001
Poisoning-related factors	2 (1–5)	2 (1–5)	0.557
Time from exposure to presentation (h)	12629 (37.8)	109 (12.0)	<0.001
Intent of poisoning	20403 (61.0)	755 (83.1)	<0.001
Unintentional, n (%)	411 (1.2)	45 (5.0)	<0.001
Intentional, n (%)	344 (0.8)	2 (0.2)	
Unknown, n (%)	26664 (79.7)	867 (95.4)	
Route of poisoning	6435 (19.2)	40 (4.4)	
Dermal, ocular, or injection, n (%)	12609 (37.7)	41 (4.5)	
Oral ingestion, n (%)	3763 (11.3)	36 (4.0)	
Inhalation, n (%)	1530 (4.6)	12 (1.3)	
Category of substances	7153 (21.4)	372 (40.9)	
A, n (%)	584 (1.7)	90 (9.9)	
B, n (%)	283 (0.8)	313 (34.4)	
C, n (%)	6123 (18.3)	37 (4.1)	
D, n (%)	1398 (4.2)	8 (0.9)	
E, n (%)			
F, n (%)			
G, n (%)			

H, n (%)			
Initial vital signs at Emergency Department	29576 (88.4)	663 (72.9)	<0.001
Systolic Blood Pressure (mmHg)	261 (0.8)	18 (2.0)	<0.001
100 – 199, n (%)	3418 (10.2)	159 (17.5)	<0.001
≥ 200, n (%)	188 (0.6)	69 (7.6)	0.004
70 – 99, n (%)	26517 (79.3)	668 (73.5)	<0.001
≤ 69, n (%)	3913 (11.7)	119 (13.1)	
Heart Rate (beat/min.)	2867 (8.6)	107 (11.8)	
70 – 119, n (%)	146 (0.4)	15 (1.7)	
30 – 69, n (%)	31193 (93.3)	747 (82.2)	
120 – 159, n (%)	68 (0.2)	8 (0.9)	
≥ 160, n (%)	2182 (6.5)	154 (16.9)	
Respiration Rate (breath/min.)	33374 (99.8)	902 (99.2)	
12 – 24, n (%)	69 (0.2)	7 (0.8)	
≤ 11, n (%)	24066 (72.0)	382 (42.0)	
≥ 25, n (%)	5491 (16.4)	177 (19.5)	
Body Temperature (°C)	3420 (10.2)	226 (24.9)	
< 39, n (%)	466 (1.4)	124 (13.6)	
≥ 39, n (%)			
Mental status, n (%)			
Alert			
Verbal response			
Pain response			
Unresponse			

Table 4. Multivariable logistic regression for the calculation of the new-Poisoning Mortality Scores (PMS) for each of category of each variable in the acute poisoning patients

	B	Points = B/0.005	Odd ratio (95% confidence interval)	p value
Demographics	Reference	0	1	<0.001
Age (years)	0.819	164	2.269 (1.650–3.120)	<0.001
< 40, n (%)	1.441	288	4.226 (2.992–5.970)	<0.001
40 – 59, n (%)	2.005	401	7.430 (5.210–10.595)	<0.001
60 – 69, n (%)	1.956	391	7.070 (4.926–10.149)	<0.001
70 – 74, n (%)	2.399	480	11.015 (7.766–15.623)	<0.001
75 – 79, n (%)	Reference	0	1	<0.001
≥ 80, n (%)	0.439	88	1.551 (1.305–1.844)	<0.001
Sex	Reference	0	1	<0.001
female	1.041	208	2.832 (2.219–3.613)	<0.001
male	1.073	215	2.925 (1.802–4.747)	0.271
Poisoning related factors	Reference	0	1	0.167
Intent of poisoning	1.01	202	2.744 (0.655–11.507)	0.495
unintention	0.591	118	1.806 (0.331–9.841)	<0.001
intention	Reference	0	1	<0.001
unknown	1.388	278	4.009 (2.522 – 6.371)	<0.001
Route of poisoning	1.821	364	6.18 (3.172 – 12.040)	<0.001
dermal, ocular, or injection	2.655	531	14.227 (10.142 – 19.956)	<0.001
oral	3.371	674	29.108 (19.326 – 43.842)	<0.001
inhalation	5.872	1174	354.892 (242.930 – 518.455)	<0.001
Category of substances	1.805	361	6.082 (2.203 – 16.793)	<0.001
A, n (%)	1.527	305	4.606 (2.064 – 10.278)	<0.001
B, n (%)	Reference	0	1	0.755
C, n (%)	-0.093	-19	0.911 (0.507–1.637)	<0.001
D, n (%)	0.731	146	2.077 (1.646–2.619)	<0.001
E, n (%)	1.909	382	6.748 (4.592–9.916)	0.001
F, n (%)	Reference	0	1	0.316
G, n (%)	0.126	25	1.134 (0.887–1.450)	0.001

H, n (%)	0.451	90	1.570 (1.189–2.074)	0.009
Vital signs at Emergency Department	0.973	195	2.647 (1.279–5.479)	<0.001
	Reference	0	1	0.992
Systolic blood pressure (mmHg)	-0.005	-1	0.995 (0.358–2.766)	<0.001
100 – 199	0.702	140	2.017 (1.581–2.574)	0.247
≥ 200	Reference	0	1	<0.001
70 – 99	0.666	133	1.947 (0.630–6.018)	<0.001
≤ 69	Reference	0	1	<0.001
Heart rate (beats/min.)	0.61	122	1.841 (1.474–2.300)	<0.001
70 – 119	1.02	204	2.773 (2.224–3.457)	
30 – 69	2.055	411	7.810 (5.737–10.632)	
120 – 159				
≥ 160				
Respiration rate (breaths/min.)				
12 – 24				
≤ 11				
≥ 25				
Body temperature (℃)				
< 39				
≥ 39				
Mental status				
Alert				
Verbal response				
Pain response				
Unresponse				

Base constant B was selected as the smallest regression coefficient in the model, which was 0.005.

The new-PMS was the sum of the point of each variable. The possible range of new-PMS was -20 to 3420 points.

Table 5. Risk groups within the derivation and validation groups

Risk group	New-PMS[a)]	Derivation cohort		Validation cohort	
		Mean predicted mortality[b)] (95% CI)	Observed mortality (%)	Mean predicted mortality (95% CI)	Observed mortality (%)
Very low	≤ 593	0.1 (0.073 – 0.074)	2/8612 (0.0)	0.1 (0.073 – 0.075)	0/2269 (0.0)
Low	594 – 786	0.2 (0.211 – 0.0214)	16/8587 (0.2)	0.2 (0.209 – 0.214)	3/2263 (0.1)
Intermediate	787 – 1047	0.6 (0.606 – 0.615)	36/8582 (0.4)	0.6 (0.595 – 0.614)	8/2017 (0.4)
High	≥ 1048	9.7 (9.345 – 10.045)	855/8571 (10.0)	8.4 (7.699 – 9.056)	124/1667 (7.4)

[a)] Sum of scores for each variable as shown in Table 4. PMS, Poisoning Mortality Score

[b)] Predicted mortality = $1/(1 + e^{-z})$, z = -9.708 +0.005*newPMS

Figures

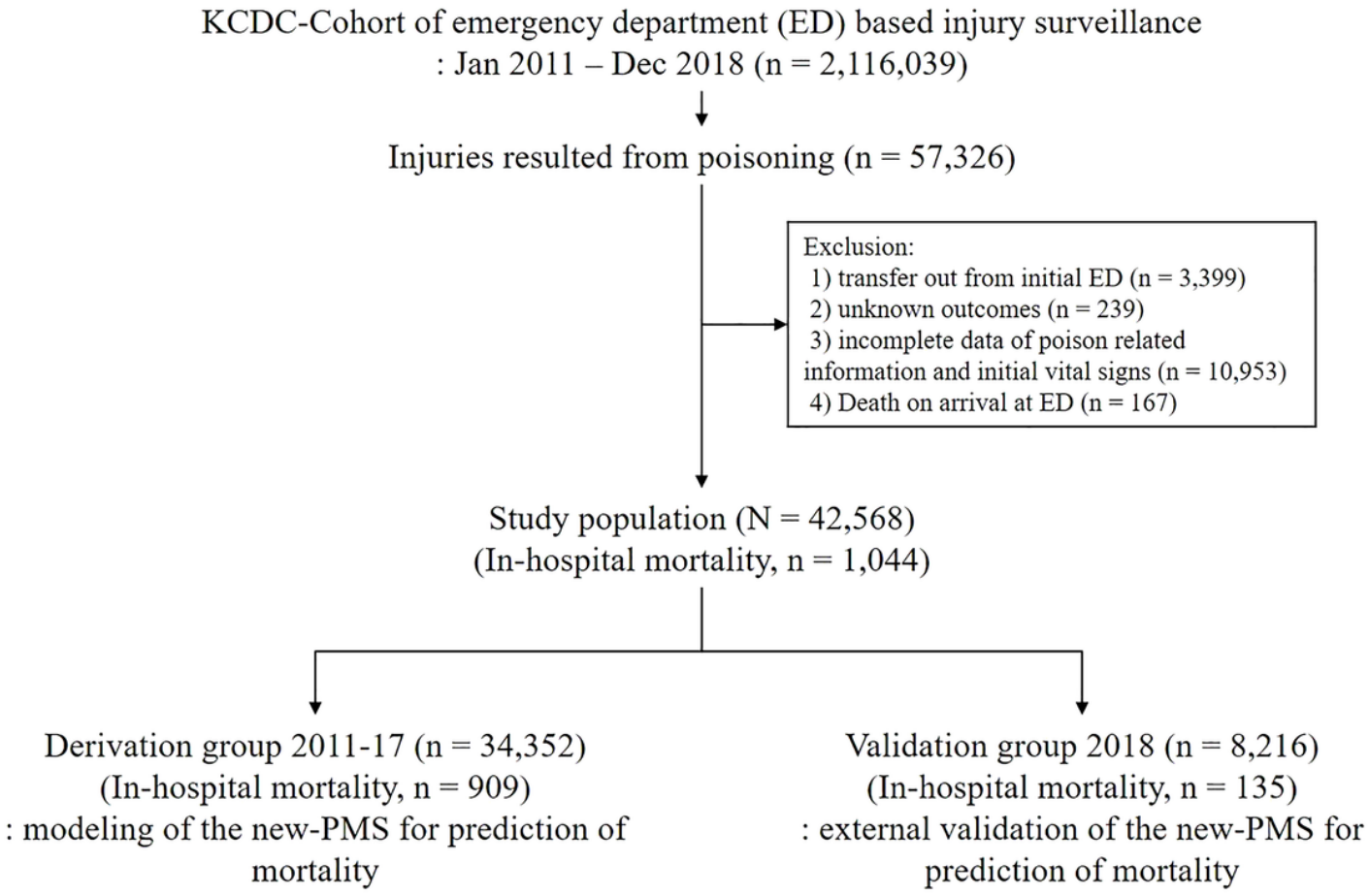

Figure 1

Selection of study patients. Of 42568 study patients, 34352 (80.7%) and 8216 (19.3%) were enrolled in the derivation and validation groups, respectively. PMS, Poisoning Mortality Score.

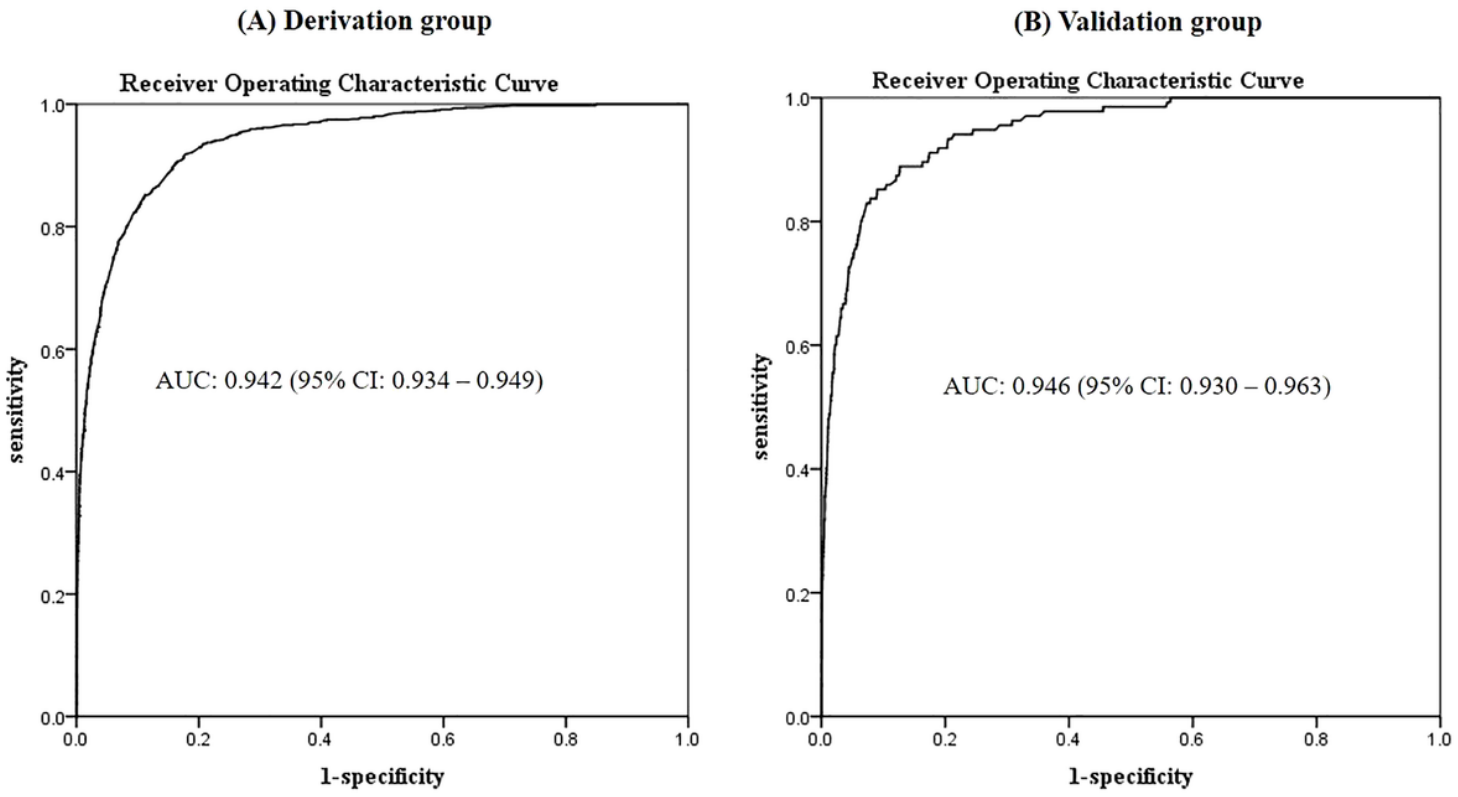

Figure 2

Receiver operating characteristic curve of the new-Poisoning Mortality Score for the prediction of in-hospital mortality in the derivation group (A) and validation group (B). The area under the curve (AUC) was 0.924 for the derivation group and 0.935 for the validation group.

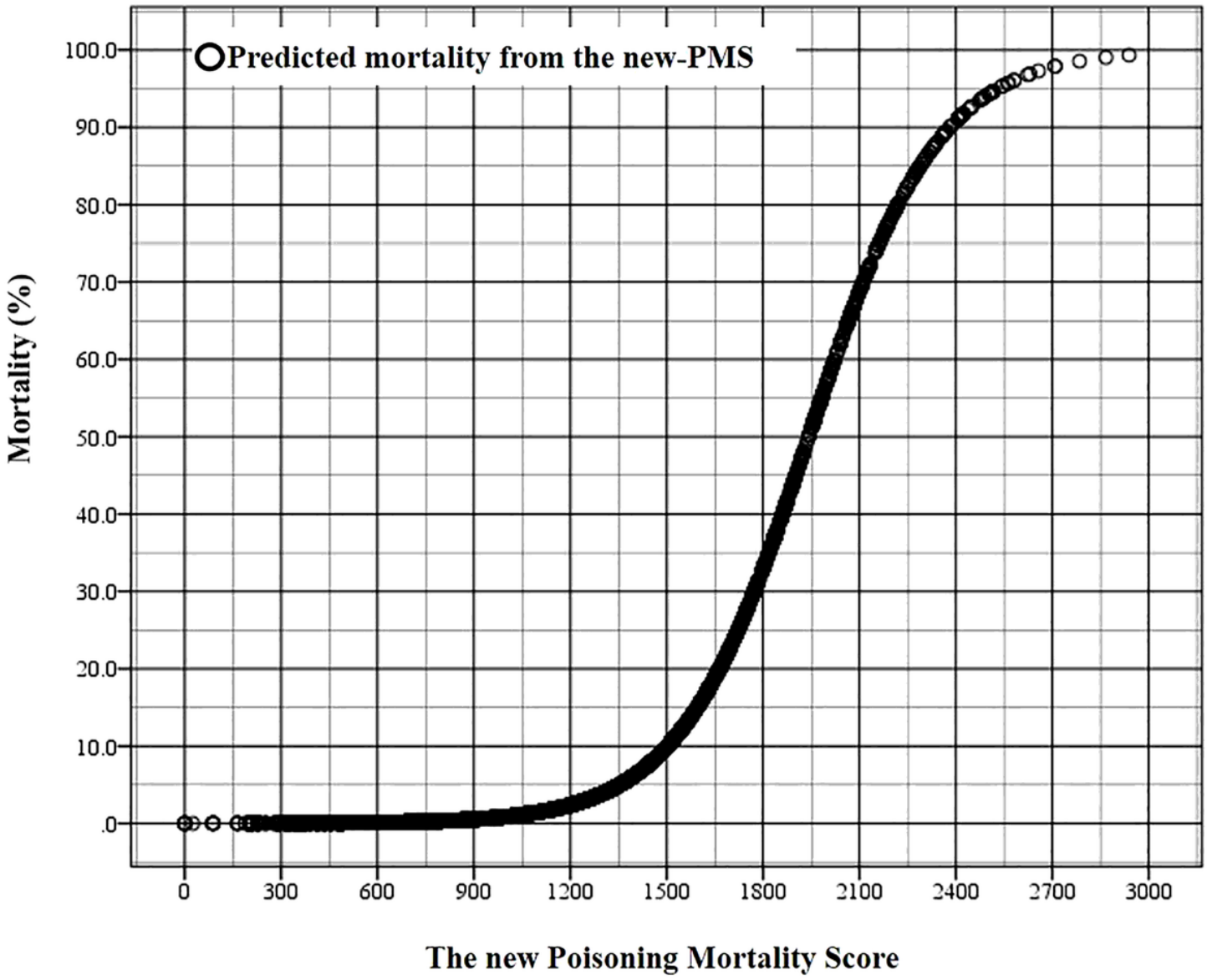

Figure 3

Mortality curve of the new-Poisoning Mortality Score (new-PMS) in the derivation group. At the new-PMS of 76 points or above, the predicted and observed mortalities increased very sharply. If early hemodynamic stabilization improves the new-PMS, this may result in the improvement of clinical outcomes. Predicted mortality = 1/(1 + e-z), z = -8.921 + 0.062 × new-PMS

Supplementary Files

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- additionalfile1.pdf