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A newly developed, easy-to-use prehospital drug-derived score compared with three conventional scores: A prospective multicenter study

Jesús Jurado-Palomo[1,2] | **José Luis Martin-Conty**[2,3,4] | **Begoña Polonio-López**[2,3,4] | **Juan J. Bernal-Jiménez**[2,3] | **Rosa Conty-Serrano**[5] | **Michele Dileone**[1,2] | **Miguel A. Castro Villamor**[6] | **Carlos del Pozo Vegas**[6,7] | **Raúl López-Izquierdo**[6,8,9] | **Cristina Rivera-Picón**[2,3] | **Francisco Martín-Rodríguez**[10] | **Ancor Sanz-García**[3,4]

[1]Hospital General Nuestra Señora del Prado, Talavera de la Reina, Spain

[2]Faculty of Health Sciences, University of Castilla la Mancha, Talavera de la Reina, Spain

[3]Technological Innovation Applied to Health Research Group (ITAS Group), Faculty of Health Sciences, University of de Castilla-La Mancha, Talavera de la Reina, Spain

[4]Evaluación de Cuidados de Salud (ECUSAL), Instituto de Investigación Sanitaria de Castilla-La Mancha (IDISCAM), Talavera de la Reina, Spain

[5]Faculty of Nursing, University of Castilla-La Mancha, Toledo, Spain

[6]Faculty of Medicine, Universidad de Valladolid, Valladolid, Spain

[7]Emergency Department, Hospital Clínico Universitario. Gerencia Regional de Salud de Castilla y León, Valladolid, Spain

[8]CIBER of Respiratory Diseases (CIBERES), Institute of Health Carlos III, Madrid, Spain

[9]Emergency Department, Hospital Universitario Rio Hortega, Gerencia Regional de Salud de Castilla y León, Valladolid, Spain

[10]Prehospital Critical Care, Emergency Medical Services. Gerencia Regional de Salud de Castilla y León, Valladolid, Spain

Correspondence
Cristina Rivera-Picón, Faculty of Health Sciences, Universidad de Castilla la Mancha. Avda. Real Fábrica de Seda, s/n 45600, Talavera de la Reina, Toledo, Spain.
Email: cristina.rivera@uclm.es

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Abstract

Introduction: The use of medications by emergency medical services (EMS) is increasing. Conventional scores are time-consuming and therefore difficult to use in an emergency setting. For early decision-making, an easy-to-use score based on the medications administered by the EMS may have prognostic value. The primary objective of this study was to develop the prehospital drug-derived score (PDDS) for 2-day mortality.

Methods: A prospective, multicenter, ambulance-based cohort study was conducted in adults with undifferentiated acute diseases treated by EMS and transferred to the emergency department. Demographic data, prehospital diagnosis data, prehospital medication and variables for the calculation of the National Early Warning Score 2 (NEWS2), Rapid Emergency Medicine Score (REMS), and Rapid Acute Physiology Score (RAPS) were collected. The PDDS was developed

Francisco Martín-Rodríguez and Ancor Sanz-García are joint last authors.

and validated, establishing three levels of risk of 2-day mortality. The predictive capability of each score was determined by the area under the curve of the receiver operating characteristic curve (AUROC) and compared using the Delong's test (*p*-value).

Results: A total of 6401 patients were included. The PDDS included age and the use of norepinephrine, analgesics, neuromuscular blocking agents, diuretics, antihypertensive agents, tranexamic acid, and bicarbonate. The AUROC of PDDS was .86 (95% CI: .816–.903) versus NEWS2 .866 (95% CI: .822–.911), $p = .828$; versus REMS .885 (95% CI: .845–.924), $p = .311$; versus RAPS .886 (95% CI: .846–.926), $p = .335$, respectively.

Conclusion: The newly developed easy-to-use prehospital drug-derived PDDS score has an excellent predictive value of early mortality. The PDDS score was comparable to the conventional risk scores and therefore might serve as an alternative score in the prehospital emergency setting.

KEYWORDS

acute disease, emergency medical services, mortality, point-of-care medication, risk assessment

1 | INTRODUCTION

Emergency medical services (EMSs) face daily life-threatening situations that require immediate identification and rapid and appropriate assistance. Early administration of an appropriate spectrum of medications, along with timely interventions, has been proven essential for the initial management and treatment of patients in these critical conditions. Furthermore, the use of medications at the prehospital level is constantly increasing.[1] Multiple studies have highlighted the importance of such actions for the stabilization of critically unwell patients, thereby improving their survival.[2] For example, studies such as that by Cudini et al.[3] highlighted the timely identification of sepsis patients in the prehospital setting, thereby supporting the initiation of prehospital antibiotic therapy in these patients. Other studies have also emphasized that the prompt administration of antibiotics is correlated with reduced mortality in sepsis patients.[4] Additionally, the study of Ho et al.[5] demonstrated the effectiveness of using vasopressin and epinephrine. There is evidence that the use of tranexamic acid (TXA) in the prehospital setting reduces mortality in trauma patients.[6]

However, despite their undeniable necessity and the significant benefits they provide in critical moments, interventions and medications administered by EMS are not without complications or side effects.[7–9] Additionally, evidence indicates that the combination of various medications increases these risks.[10,11] Therefore, it is reasonable to assess the key role of medications in the prehospital setting. To date, no studies have been conducted to analyse the impact of the administration of multiple medications by the EMS on patient mortality.

Moreover, the potential predictive role of a score derived from the use of these medications for short-term mortality in undifferentiated prehospital patients is unknown. Such a score would be even simpler than those derived from early warning system scores (EWSs),[12,13] as it would only include age and dichotomous variables, that is, the use or nonuse of certain medications. Therefore, the aim of this work was to assess the potential of a risk score based on medications administered by EMS providers. The main objective was to develop and validate the prehospital drug-derived score (PDDS) for 2-day mortality prediction and, second, to establish three levels of risk (low, intermediate, and high risk of mortality) on the basis of the points of the score. Additionally, the study aims to highlight the predictive value of this simple risk score, given that medication use is not known. Conventional scores are often time-consuming and challenging to implement in emergency settings. For timely decision-making, a straightforward, medication-based score could offer significant prognostic value. Moreover, this study compares the new score with existing risk scores, which, despite being more comprehensive, are not as practical. This comparison highlights the potential benefits of using a simple, medication-based score in urgent prehospital situations.

2 | METHODS

2.1 | Study design and setting

A prospective, multicenter, ambulance-based cohort study was conducted in adults with undifferentiated acute diseases who were treated by EMS and transferred to the emergency department (ED).

The research was conducted in three Spanish provinces—Salamanca, Segovia and Valladolid—encompassing a population of 995,137 inhabitants. The study involved six advanced life support (ALS) units, thirty-eight basic life support (BLS) units, and four hospitals. Resource management was overseen by the public health system and facilitated by the Emergency Coordination Center 1–1–2. Each BLS unit was staffed by two emergency medical technicians (EMTs), whereas the ALS units were equipped with an emergency registered nurse (ERN) and a physician. The EMS teams consistently operated in accordance with established guidelines for both basic and advanced life support. Further details regarding the structure and function of the EMS can be found in Appendix S1. The standard equipment for the ALS units included a pharmaceutical inventory of 83 medications, detailed in Table S1.

The study was reviewed and approved by the institutional review board of the Public Health Service (reference: PI-049-19 and PI-GR-19-1258). The research protocol was registered with the WHO International Clinical Trials Registry Platform (ISRCTN48326533 and ISRCTN49321933). We followed the guidelines of the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement (Appendix S1).

2.2 | Population

Adults (≥18 years) with undifferentiated acute diseases who were transferred to the ED between January 2019 and July 2022 were consecutively recruited for the study. To be included in the study, the case was always assessed by an ALS physician. Data were collected continuously via convenience sampling to minimize bias.

On the basis of the structured clinical evaluation and available on-scene complementary diagnostic tests, the need for transfer to the ED, either in BLS or ALS, was subsequently determined by the ALS physician on scene. Patients who died upon arrival, paediatric, obstetric, cardiac arrest or palliative care patients (as per existing documentation) were excluded from this study. Additionally, patients with incomplete follow-up data and those who did not provide informed consent were also excluded. Informed consent was initially sought by the ERN during ALS contact. If not possible onsite, it was pursued by a family member or legal guardian. The consent form is available in Appendix S1.

2.3 | Outcomes

The primary outcome of the study was 2-day in-hospital mortality from all causes, which was assessed from the first ALS contact with the patient at the scene. This space of time was chosen for two reasons: premature die-offs were directly associated with reasons for EMS assistance; in general, scoring systems are validated to predict potential premature worsening risk.

2.4 | Data collection

Epidemiological variables (sex at birth and age) were collected from the ERNs. Additionally, not all EMS providers are authorized to dispense certain medications, as this requires prior authorization from the local medical supervisor. Details on the quantity and type of medications provided were compiled according to the following classification: anticholinergics, antiarrhythmics, antibiotics, anticoagulants, anticonvulsants, antidotes, antiemetics, antihistamines, antihypertensives, antiplatelet agents, antipsychotics, anxiolytics, beta-blockers, bicarbonate, bronchodilators, corticosteroids, diuretics, epinephrine, fibrinolytics, gastric protectors, glucose, hypnotics, insulin, ions, major analgesics (fentanyl, ketamine, meperidine, morphine, and tramadol, all intravenous administration), minor analgesics (dexketoprofen, ketorolac, metamizole and paracetamol, all oral administration), neuromuscular blocking agents, norepinephrine, TXA and vasodilators.

After reviewing the electronic medical records at the 2-day follow-up after the prehospital index event, an investigator assigned to each hospital collected data on mortality and comorbidities to calculate the age-adjusted Charlson comorbidity index and admission to the critical care units.

The data were stored in a dedicated electronic database, with patient identifiers anonymized through logical, range, and consistency tests. The data security measures included individual passwords, dual authentication, and database partitioning, which were restricted to access by only the principal investigator (PI) and data manager. EMS providers did not have access to hospital follow-up data, and hospital researchers were unaware of the administered medications. The categorization on the basis of the administered medications was exclusively performed by the principal investigator and the data manager.

2.5 | Statistical analysis

The Mann–Whitney *U* test or chi-square test, when appropriate, was used for the presentation of the descriptive results and for the associations between the predictors and the outcomes. Absolute values and percentages were used for categorical variables, and median interquartile ranges (IQRs) were used for continuous variables because they did not follow a normal distribution. The data collection, missing value handling, and sample size calculations can be found in Appendix S1.

The first objective was to develop and validate the risk score. First, the cohort was split into training and validation cohorts by maintaining the proportion of the outcome in 2/3 and 1/3 of the patients, respectively. Second, all the medications administered, age and sex were fitted in a logistic regression model. The statistically significant variables were considered for the score, and the weight of each variable, that is, the points given to each category (all the variables included were categorical), was derived from the beta coefficients from the logistic regression, rounded to the integer. The final score of each patient was the sum of all the points given to each variable considered in the score. Third, two different methods were used to validate the score performance, exclusively using the validation cohort: (i) The discriminative power of the model was assessed by the area under the curve of the receiver operating characteristic (AUROC) curve analysis, including the 95% confidence intervals (CIs). All 95% CIs were obtained by bootstrapping (2000 iterations). The p value of the hypothesis test (H0: AUROC = .5) was also provided (note that AUROC = .5 means no predictive capacity, .5–.7 poor, .7–.9 excellent, and .9–1 perfect predictive capacity).[14] The following parameters of the AUROC curve were assessed: specificity (sp), sensitivity (sen), positive predictive value, negative predictive value, positive likelihood ratio, and negative likelihood ratio. The maximum potential effectiveness achieved by the score, the Youden index, was also reported. The score will be compared with those of other EWs via a direct AUROC comparison performed via Delong's test. (ii) Calibration was performed by calculating the calibration curve, that is, plotting the predicted versus observed probability of the outcome and determining several metrics associated with calibration (further details in Appendix S1). Fourth, on the basis of the predicted probability curve, low-, intermediate- and high-risk mortality groups were established. That is, the three phases (lag, exponential and stationary) of the sigmoid curve resulting in the predicted probability curve were used to determine the ranges of the score points of each group.

The data were analysed via our own codes and basic functions in R, version 4.2.2 (R Foundation for Statistical Computing, Vienna, Austria).

3 | RESULTS

A total of 6401 patients were enrolled in the final cohort analysis (Figure 1). The 2-day mortality rate was 3.6% (232 patients). The median age of the nonsurvivors was 79 years (IQR: 66–86), with a statistically significant difference in the number of nonsurvivors aged 50–74 years and ≥75 years versus survivors ($p < .05$ and $p < .001$, respectively); 41.8% of the nonsurvivors were females (97 patients), with no statistically significant difference versus survivors ($p = .905$), and sex was not included in the score since no differences were found. The mean number of medications used was double that used by the survivors (2 (IQR: 1–3) for survivors versus 4 (IQR: 3–6) for nonsurvivors, $p < .001$). Compared with that among survivors, intensive care unit admission was significantly greater among nonsurvivors (40.9% vs. 8.93%, $p < .001$). The admission rates to the acute cardiovascular care unit were not significantly different between the survivor and nonsurvivor groups ($p = .172$) (Table 1).

Compared with survivors, nonsurvivors reported greater use of norepinephrine (19.8%, $p < .001$), major analgesics (56.0%, $p < .001$), minor analgesics (24.6%, $p < .01$), neuromuscular blocking agents (33.2%, $p < .001$), diuretics (17.7%, $p < .001$), TXA (8.19%, $p < .001$) and bicarbonate (12.9%, $p < .001$) (Table 2).

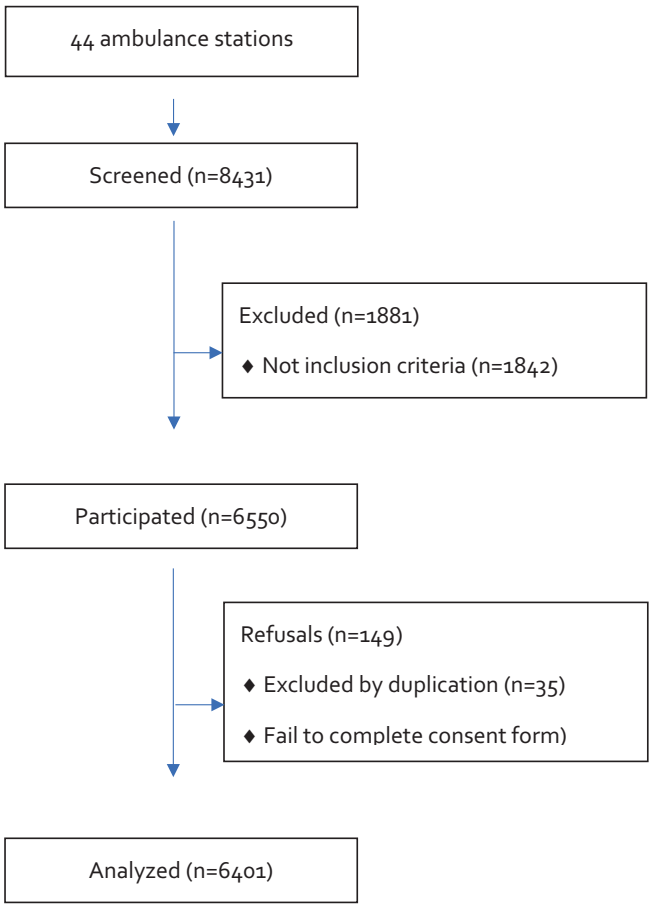

FIGURE 1 Study flowchart.

TABLE 1 Baseline patient characteristics according to mortality.

No. (%) with data[a]	Survivors $N = 6061$	Non survivors $N = 232$	Odds ratio [95%CI]	*p* Value
Epidemiological variables				
Age groups, year				
18–49	1404 (23.2%)	23 (9.91%)	Ref.	Ref.
50–74	2406 (39.7%)	67 (28.9%)	1.69 [1.06; 2.79]	.026
≥75	2251 (37.1%)	142 (61.2%)	3.83 [2.50; 6.13]	<.001
Sex at birth, female	2511 (41.4%)	97 (41.8%)	1.02 [.78; 1.32]	.905
NIMV	179 (2.95%)	47 (20.3%)	8.36 [5.82; 11.8]	.000
IMV	209 (3.45%)	80 (34.5%)	14.7 [10.8; 19.9]	.000
Suspected prehospital diagnoses				
Infection	346 (5.71%)	44 (19.0%)		
Endocrine	146 (2.41%)	7 (3.02%)		
Nervous system	1183 (19.5%)	45 (19.4%)		
Cardiovascular	2302 (38.0%)	54 (23.3%)		
Respiratory	439 (7.24%)	23 (9.91%)		
Digestive	252 (4.16%)	7 (3.02%)		
Trauma	838 (13.8%)	46 (19.8%)		
Intoxication	486 (8.02%)	6 (2.59%)		
Anaphylaxis	68 (1.12%)	0 (.00%)		
Hospital outcomes				
aCCI, points	4.00 [1.00; 7.00]	7.00 [4.00; 10.0]	1.20 [1.16; 1.24]	<.001
Hospital admission	3133 (51.7%)	228 (98.3%)	51.2 [21.8; 169]	.000
ICU admission	541 (8.93%)	95 (40.9%)	7.07 [5.35; 9.31]	.000
ACCU admission	487 (8.04%)	13 (5.60%)	.69 [.37; 1.16]	.172
Lengths of stays	2.00 [.00; 8.00]	1.00 [.00; 2.00]	.78 [.73; .83]	<.001

Abbreviations: aCCI, age–Charlson comorbidity index; ACCU, acute cardiovascular care unit; ICU, intensive care unit; IMV, invasive mechanical ventilation; NIMV, noninvasive mechanical ventilation.

[a]Values expressed as total number (fraction) and medians [25th percentile–75th percentile], as appropriate.

3.1 | Developed score

The developed PDDS included the dichotomic variables described in Table 3, which included age 50–74 years, age ≥75 years, and the following intravenous medications: norepinephrine, minor analgesics, major analgesics, neuromuscular blocking agents, diuretics, antihypertensive agents, TXA, and bicarbonate. The points given to each category are also described in Table 3. The resulting odds ratios and *p* values of the logistic regression analyses are shown in Table S2.

3.2 | PDDS validation

The performance of the model is shown in Figure 2A. The AUROC reached .86 (95% CI: .817–.903). The PDDS score points versus the probability of death are shown in Figure 2B. As the mortality score increased, the predicted probability was described by a sigmoid curve. Further details regarding the performance of the model can be found in Table S3. The calibration results (Figure 2C) supported the discriminative power of the model. The 2-day mortality rate was 3.6% (232 patients), demonstrating that the PDDS has high predictive ability for this specific outcome.

3.3 | Risk groups based on the PDDS

Finally, the low-, intermediate-, and high-risk mortality groups were established on the basis of Figure 2B. The lag phase ranged from 0 to 2, the exponential phase ranged

TABLE 2 Prehospital drugs administered according to mortality.

No. (%) with data[a]	Survivors *N* = 6061	Non survivors *N* = 232	Odds ratio [95% CI]	*p* Value
Prehospital drugs administration				
Number of drugs used	2.00 [1.00; 3.00]	4.00 [3.00; 6.00]	1.78 [1.67; 1.90]	<.001
Antibiotic	15 (.25%)	1 (.43%)	1.98 [.08; 9.83]	.568
Anticholinergics	156 (2.57%)	19 (8.19%)	3.40 [2.01; 5.45]	<.001
Antiplatelet agent	525 (8.66%)	12 (5.17%)	.58 [.31; 1.00]	.052
Norepinephrine	59 (.97%)	46 (19.8%)	25.1 [16.6; 37.9]	.000
Minor analgesics	1062 (17.5%)	57 (24.6%)	1.54 [1.12; 2.07]	.008
Mayor analgesics	1036 (17.1%)	130 (56.0%)	6.18 [4.73; 8.09]	.000
Hypnotic	523 (8.63%)	102 (44.0%)	8.31 [6.30; 10.9]	.000
Neuromuscular blocking agent	200 (3.30%)	77 (33.2%)	14.6 [10.7; 19.7]	.000
Anticonvulsant	309 (5.10%)	10 (4.31%)	.85 [.42; 1.54]	.617
Anxiolytic	421 (6.95%)	1 (.43%)	.07 [.00; .29]	<.001
Bronchodilator	557 (9.19%)	47 (20.3%)	2.52 [1.79; 3.48]	<.001
Corticosteroid	511 (8.43%)	37 (15.9%)	2.07 [1.42; 2.94]	<.001
Gastric protector	645 (10.6%)	22 (9.48%)	.89 [.55; 1.35]	.588
Antiemetic	1236 (20.4%)	56 (24.1%)	1.24 [.91; 1.68]	.171
Diuretic	359 (5.92%)	41 (17.7%)	3.42 [2.37; 4.82]	<.001
Antiarrhythmic	168 (2.77%)	6 (2.59%)	.95 [.37; 2.00]	.913
Beta-blocker	142 (2.34%)	6 (2.59%)	1.13 [.44; 2.38]	.770
Antihypertensive	123 (2.03%)	8 (3.45%)	1.76 [.78; 3.42]	.162
Tranexamic acid	62 (1.02%)	19 (8.19%)	8.67 [4.96; 14.5]	<.001
Insulin	171 (2.82%)	20 (8.62%)	3.27 [1.96; 5.18]	<.001
Antidote	355 (5.86%)	5 (2.16%)	.37 [.13; .80]	.009
Ions	66 (1.09%)	10 (4.31%)	4.14 [1.97; 7.82]	.001
Bicarbonate	72 (1.19%)	30 (12.9%)	12.4 [7.79; 19.2]	.000
Antipsychotic	38 (.63%)	2 (.86%)	1.48 [.22; 4.87]	.619

[a]Values expressed as total number (fraction) and medians [25th percentile-75th percentile], as appropriate.

from 3 to 5, and the stationary phase ranged from 6 to 9. These ranges corresponded to low (4991 patients), intermediate (1255 patients), and high risk of mortality (47 patients), representing 1.08% (54 patients), 12.3% (154 patients), and 51.1% (32 patients) of the total mortality, respectively. Table S4 shows the characteristics of each risk group. The mortality rates were 1.08% for the low-risk group, 12.3% for the intermediate-risk group, and 51.1% for the high-risk group.

3.4 | PDDS vs. other EWS scores

The PDDS was compared with the National Early Warning Score 2 (NEWS2), Rapid Emergency Medicine Score (REMS) and Rapid Acute Physiology Score (RAPS). No significant differences were found in the AUROC (Delong's test $p > .05$) (Table 4), and the AUROCs were .860 (95% CI: .816–.903), .866 (.822–.911), .885 (.845–.924), and .886 (.846–.926) for the PDDS, NEWS2, REMS and RAPS, respectively.

4 | DISCUSSION

To the best of our knowledge, this is the first study to evaluate and validate a risk score based on medications administered by EMS providers specifically for the prediction of 2-day mortality. The results revealed the development of the PDDS, demonstrating its predictive value (AUROC = .86 (95% CI: .817–.903)). This approach also allowed us to characterize patients with low, intermediate, and high risks of mortality on the basis of the obtained scores. Our findings highlighted that variables such as advanced age and the use of specific medications (norepinephrine, analgesics, neuromuscular blocking agents,

TABLE 3 Prehospital administered drug score.

	Points		
	0	1	2
Age 50–74 years	No	Yes	
Age ≥75 years	No		Yes
Norepinephrine	No		Yes
Minor analgesics	No	Yes	
Major analgesics	No	Yes	
Neuromuscular blocking agent	No	Yes	
Diuretic	No	Yes	
Antihypertensive	No	Yes	
Tranexamic acid	No	Yes	
Bicarbonate	No		Yes

diuretics, antihypertensives, TXA and bicarbonate) were risk factors for mortality. Furthermore, it is worth noting that the use of multiple medications indicates a worse outcome.

Patients with intermediate and high risk of mortality received a greater number of medications. This finding aligns with the results of several studies that showed that polypharmacy is associated with a greater risk of mortality.[10,11] Drug administration in the low-risk group was considerably lower than that in the other groups. Among the low-risk group patients, there was slightly more frequent administration of antiemetics, antiplatelets, anxiolytics, minor analgesics and major analgesics. Notably, no norepinephrine was administered to any of the subjects in this group. In the intermediate-risk group, the most frequently administered medications were major analgesics and minor analgesics. Patients in this category present with a variety of pathologies, primarily diseases of the circulatory system, trauma and infectious disease. In the high-risk group, the medications included in the proposed score were used more frequently than in the other groups, and the most commonly used medications were major analgesics, norepinephrine, hypnotic muscle relaxants and bicarbonate. There was also an increase in the administration of minor analgesics and TXA, although to a lesser extent. This medication pattern is consistent when the conditions of this group are considered: nearly half of the patients were trauma cases, whereas a significant proportion had diseases related to the circulatory system.

Thus, the use of multiple medications and more invasive medications, such as norepinephrine, neuromuscular blockers, and bicarbonate, was significantly associated with a greater risk of mortality. These findings suggest that individuals in this group are likely to face more severe conditions and have a worse prognosis. These findings are consistent with previous studies indicating that polypharmacy and the use of invasive medications are linked to unfavourable health outcomes.[10,11]

Regarding the medications included in the PDDS, the literature suggests that norepinephrine is a vasoactive agent commonly used in the management of septic shock and cardiogenic shock, indicating a serious underlying disease. The need for norepinephrine suggests that hypotension does not respond to fluids, which is often associated with high mortality.[15–18] On the other hand, the administration of analgesics, both minorly and primarily, usually indicates the presence of moderate to severe pain. Major analgesics are associated with intense pain, reflecting greater clinical severity.[19] However, Friesgaard et al.[20] reported that available evidence for the prehospital administration of major analgesics to relieve acute pain is scarce. Furthermore, their administration is associated with a greater risk of short-term adverse events.[20,21] Cook et al.[22] argued that the use of neuromuscular blocking agents is primarily indicated for orotracheal intubation and for the management of critical patients requiring mechanical ventilation. The use of diuretics may indicate acute episodes of decompensation in these diseases, which could suggest a more complicated prognosis in advanced stages.[23] Regarding the administration of antihypertensives, various authors have demonstrated that the use of these medications may indicate the presence of chronic hypertension. Such decompensated hypertension can lead to acute cardiovascular events such as myocardial infarctions or strokes, increasing the risk of mortality.[24] TXA is used for the management of significant bleeding, including major trauma. Its inclusion reflects the severity of the bleeding and the potential need for additional interventions to control it.[25,26] Finally, bicarbonate is administered in cases of severe metabolic acidosis.[27] Burger et al.[28] reported that metabolic acidosis is not a benign condition and is an underlying disorder that must be corrected to minimize morbidity and mortality.

Therefore, the medications included in the PDDS demonstrate significant clinical relevance, that is, they are frequently used in severe and critical situations. This underscores the importance of the score developed in the current study, which is specifically based on the use of medications administered by EMS providers to predict mortality. This provides an innovative framework for assessing the direct impact of prehospital interventions on patient outcomes. Not all EMS systems have the pharmacological toolkit available in the EMS under analysis. However, compared with previous studies that evaluated individual medications, our approach of considering multiple medications in an integrated score provides a more comprehensive and accurate assessment of prehospital mortality risk. This is crucial for improving risk stratification and early intervention in critical patients.

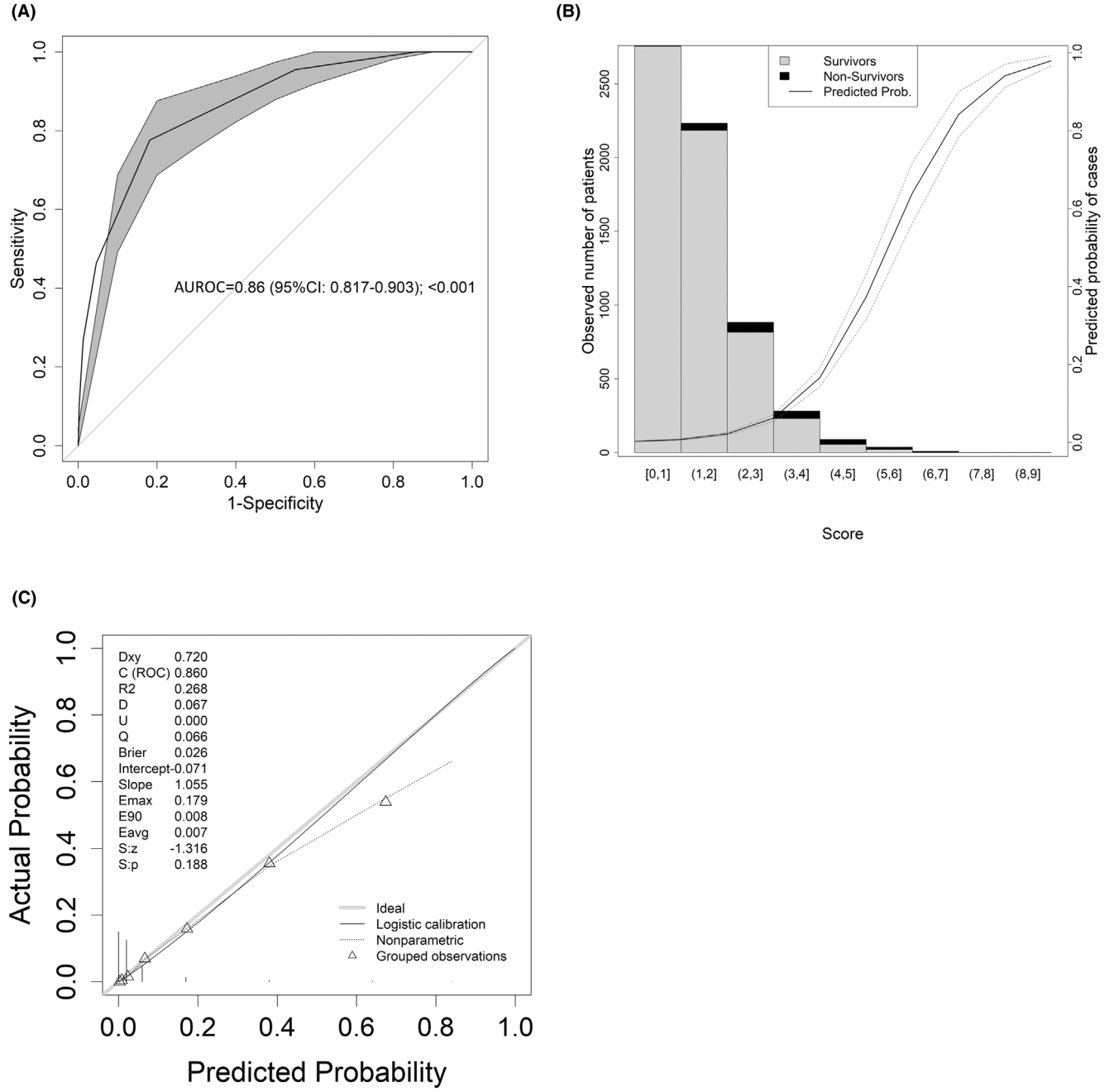

FIGURE 2 Performance of the model (A), distribution of patient outcomes according to the score points (B). Calibration curve (C).

In line with this, as we have previously indicated, there are established scores such as the NEWS, RAPS, and REMS, which assess patients on the basis of physiological variables, but none of them incorporate the specific medication variables used in emergencies. In this context, our research not only enhances these existing tools but also raises significant questions about how the selection and administration of medications can improve risk prediction systems in the prehospital environment. The direct comparison of the performance between the abovementioned physiological-based scores did not reveal a significant difference. This, at first glance, could be interpreted as a PDDS drawback; however, two points arise that could demonstrate the relevance of our score: (i) This score is exclusively based on the assessment of binary variables (yes or no answer to the use of a particular medication); therefore, it decreases the probability of mistakes when recording the information compared with the numerical variables considered in the physiological-based scores and enables a quick calculation. (ii) On the other hand, the PDDS also includes age among its variables. This inclusion is considered very valuable, as some studies have shown that age is a risk factor associated with the severity of

TABLE 4 Delong's test-derived pvalue from the comparison between the area under the receiver operating characteristics of the different scores. The diagonal represents the AUC and the 95% confidence interval.

	PDDS	NEWS2	REMS	RAPS
PDDS	.860 (.816–.903)	.828	.311	.335
NEWS2		.866 (.822–.911)	.435	.367
REMS			.885 (.845–.924)	.953
RAPS				.886 (.846–.926)

Abbreviations: NEWS2, National Early Warning Score 2; PDDS, Prehospital drug-derived score; RAPS, Rapid Acute Physiology Score; REMS, Rapid Emergency Medicine Score.

disease and mortality.[29] In this context, authors such as Pirneskoski et al.[30] have argued that the NEWS does not include age among its parameters. The authors, through a retrospective study, showed that age should be considered an additional factor to the NEWS, thus improving its performance in predicting short-term mortality in a prehospital setting. These findings align with the results of our study, which show that advanced age is a significant indicator of a greater risk of mortality.

5 | STRENGTHS AND LIMITATIONS

In short, current scores for prehospital settings assess the severity of illness on the basis of deviations from various physiological variables. However, no study has developed tools that evaluate the impact of medication administered during prehospital care on mortality. This highlights the significance of our study, which demonstrates how pharmacological intervention can significantly influence patient outcomes. Moreover, our proposed score is easier to collect since it only includes dichotomic variables rather than those scores requiring vital signs. In this sense, in emergency situations, physiological parameters may suffer from significant changes within very short periods. This means that the results obtained from scores based solely on these measures can vary considerably depending on the time of their application, whether upon arrival, during assistance, or during patient transport. This variability underscores the need for our score, which, by incorporating the assessment of the impact of medication, provides a more stable and predictive perspective on the risk of mortality.

The high predictive capacity of the PDDS, which provides reliable and precise predictions, is one of the main strengths of this study. This effectiveness is notably complemented by the simplicity of the variables, since the binary nature of its components converts the PDDS into an easy-to-use score. All of these factors allow for quick and efficient categorization of mortality risk. In prehospital settings, where time is a critical factor, having a tool that combines high predictive accuracy with agile and straightforward implementation represents a significant advancement.

Our study was not without limitations. First, the data extractors were not masked. To minimize possible confounding, the EMS providers did not have access to the hospital data; conversely, the ED investigators did not have access to the prehospital follow-up data. Only the data manager and the IP had full access to the master database. Second, a convenience sample was used. To avoid bias, data were collected uninterruptedly at 24/7/365 in several provinces, in urban and rural locations, and with different ambulance stations and hospitals. Additionally, not all EMS systems have the pharmacological toolkit available in the EMS under analysis. On the other hand, not all EMS providers are authorized to dispense determined medications, requiring prior authorization from the local medical supervisor. This fact may make the generalization of the proposed score difficult, and it should first be validated in EMS systems comparable to the one studied. Finally, the study did not assess the use of supplemental oxygen, which is a critical medication in emergency care. Retrieving comprehensive data on oxygen use across different EMS systems can be challenging and time-consuming. Therefore, the absence of oxygen data may limit the comprehensive understanding of medication practices in prehospital settings. Notably, these results were developed without minors and patients suffering cardiac arrest in the studied cohort owing to particularities of the mentioned patients, which usually required the development of specific scores. Therefore, this point should be considered when interpreting the results.

6 | CONCLUSIONS

This study successfully developed and validated a predictive score for 2-day mortality, which classifies patients into three risk categories, low, intermediate, and high, on the basis of the medications administered during prehospital

care. The primary outcome, 2-day in-hospital mortality, demonstrated that the PDDS has high predictive ability, with an AUROC of .86. This result was equivalent to that derived from other EWSs. The validation of this tool highlights its clinical significance by enabling EMS providers to conduct more accurate risk stratification. Consequently, it supports more informed decision-making regarding patient management and referral in emergency situations and, therefore, might serve as a valuable alternative to traditional risk scores in the pre-hospital emergency setting.

AUTHOR CONTRIBUTIONS

Jesús, Jurado-Palomo, Cristina Rivera-Picón, Ancor Sanz-García and Francisco Martín-Rodríguez conceptualized the project, managed and coordinated the project, assisted with the design of the methodology, analysed the data and prepared the initial and final drafts of the manuscript. Ancor Sanz-García takes responsibility for the data and their analysis. José Luis Martin-Conty, Begoña Polonio-López, Juan J. Bernal-Jiménez, Rosa Conty-Serrano, Michele Dileone, Miguel A. Castro Villamor, Carlos del Pozo Vegas and Raúl López-Izquierdo contributed to the management and coordination of the project, assisted with the design of the methodology, and helped review the manuscript. José Luis Martin-Conty, Begoña Polonio-López, Juan J. Bernal-Jiménez, Rosa Conty-Serrano, Michele Dileone, Miguel A. Castro Villamor, Carlos del Pozo Vegas and Raúl López-Izquierdo conceptualized the project and helped review and comment on the initial and final drafts of the manuscript. All the authors performed a critical review and approved the final manuscript for interpretation of the data and important intellectual input.

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CONFLICT OF INTEREST STATEMENT

All the signing authors meet the requirements of authorship. All the authors have no conflicts of interest. On behalf of the other authors, the corresponding author guarantees the accuracy, transparency, and honesty of the data and information contained in the study; that no relevant information has been omitted; and that all discrepancies between authors have been adequately resolved and described.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

PATIENT AND PUBLIC INVOLVEMENT

There was no patient or public involvement.

ORCID

José Luis Martin-Conty https://orcid.org/0000-0001-8579-2323
Cristina Rivera-Picón https://orcid.org/0000-0001-7031-2585

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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