

## ORIGINAL ARTICLE

## Prognostic value of metabolic parameters measured by first responders attending patients with severe trauma: associations with the New Injury Severity Score and mortality

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**Background and objective.** Patients with severe or potentially severe trauma must be identified early, a challenge in prehospital settings. This study aimed to analyze the possible diagnostic and prognostic usefulness of analytical markers recorded in the early moments of care.

**Methods.** Observational study of information extracted from the prospective multicenter Code Trauma database for 2016-2019, excluding data for isolated head injuries. Using the New Injury Severity Score (NISS), we classified cases into 4 levels of severity. NISS and mortality were considered the dependent variables in inferential analyses. We calculated the areas under receiver operating characteristic curves, identified optimal cutoff points (Youden index), and calculated positive (PPV) and negative predictive values.

**Results.** Of the 1039 trauma patients in the registry, 709 were included in the study. Their mean (SD) age was 40.4 (17.3) years, and 77.3% were men. Motorcycle accidents were the most common causes of trauma (in 21%), and mortality was 12.1%. Lactate concentration, pH, PCO<sub>2</sub>, hemoglobin concentration, hematocrit, and blood sugar were significantly associated with severity and mortality. The PPVs corresponding to pH for the 4 NISS score groups (34-41, 42-49, 50-59, and ≥ 60) and mortality, respectively, were 61.2, 64.1, 70.7, 62.2, and 66.6. The PPVs of traditionally used clinical variables were lower.

**Conclusions.** Patients with more severe trauma had lower pH values and higher PCO<sub>2</sub>, lactate, and base excess values. PCO<sub>2</sub>, pH, and blood sugar findings were the best predictors of severity. Metabolic variables are better predictors than traditionally recorded hemodynamic variables.

**Keywords:** Wounds and injuries. Trauma severity indices. Prognosis. Emergency medical services. Blood gas analysis.

### *Valor pronóstico de los parámetros metabólicos medidos en la asistencia inicial a pacientes con trauma grave: asociación con la puntuación de la escala NISS y la mortalidad*

**Objetivos.** En entornos de emergencia prehospitalarios, la detección temprana de un paciente con trauma grave o potencialmente crítico es un desafío. El objetivo es analizar las posibilidades diagnósticas y pronóstico de los parámetros analíticos obtenidos en los primeros momentos de la asistencia inicial.

**Método.** Estudio observacional multicéntrico de la base de datos prospectiva "Código Trauma" de 2016-2019 excluyendo el trauma craneoencefálico aislado. La evaluación de las lesiones se realizó utilizando el New Injury Severity Score (NISS). Los pacientes fueron clasificados en 4 grupos según nivel de gravedad. Para el análisis inferencial, las puntuaciones NISS y el resultado de mortalidad se consideraron variables dependientes. Se realizó el análisis de la curva ROC, puntos de corte óptimos mediante el índice de Youden y se calcularon los valores predictivos positivo (VPP) y negativo.

**Resultados.** De los 1.039 pacientes traumatizados del registro, 709 fueron incluidos en el estudio, con una edad media de 40,4 años (DE 17,3), 77,3% eran varones, el mecanismo lesional principal accidentes de moto (21%) y la mortalidad del 12,1%. El pH, lactato, pCO<sub>2</sub>, hemoglobina, hematocrito y glucemia influyeron significativamente en gravedad y mortalidad. El VPP de mortalidad para pH fue 61,2, 64,1, 70,7, 62,2 y 66,6 para los grupos de NISS 34-41, 42-49, 50-59 y ≥ 60 puntos la mortalidad, respectivamente. Las variables clínicas clásicas obtuvieron valores más bajos.

**Conclusiones.** Los pacientes con mayor gravedad presentaron menor pH y concentraciones más altas de pCO<sub>2</sub>, lactato y exceso de bases. El pH, la pCO<sub>2</sub> y la glucemia tuvieron la mayor capacidad predictiva de gravedad. La capacidad predictiva de los valores metabólicos es superior a la de los valores hemodinámicos clásicos.

**Palabras clave:** Trauma. Índices de gravedad del trauma. Pronóstico. Servicios médicos de emergencia. Análisis de gases en sangre.

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All authors have confirmed their authorship in the document of author responsibilities, publication agreement, and assignment of rights to EMERGENCIAS.

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#### Article Information:

Received: 13-10-2022

Accepted: 10-11-2022

Online: 21-12-2022

#### Editor in Charge:

Agustín Julián Jiménez

## Introduction

Trauma is the leading cause of death and disability in people under 40.<sup>1,2</sup> It is considered as crucial as cardiac arrest, acute coronary syndrome, or stroke. Given its time-dependent nature, its early management is a fundamental prognostic element. The latter is relevant for both specialized hospital units and on-site emergency care.<sup>3</sup>

In recent decades, one of the most explored research fields has been the search for severity assessment factors and scales to anticipate pathological changes and, therefore, enable better treatment.<sup>4,5</sup> In the out-of-hospital emergency setting, early detection of critical or potentially critical patients is a fundamental challenge, particularly in trauma patients. Since the description of the “golden hour” concept, efforts are towards shortening hospital arrival times to reach the necessary resources early, which includes the management of hospital early warning with alerts to those services that will intervene in the immediate care of the patient (intensive care unit, blood bank, operating room, etc.), without detriment to the quick actions that must be performed on-site.

There are anatomical and physiological scales<sup>6,7</sup> that attempt to predict mortality in these patients but in some cases, they are not very reliable, and in others, they are challenging to apply due to the lower diagnostic capacity that is usually available in the out-of-hospital setting, especially in the absence of the most sophisticated imaging techniques. The prognostic factors related to mortality in literature are often heterogeneous and contradictory.

There are still several questions about the physiological changes that occur right after trauma, which we could consider as the microhemodynamics of the process. We should examine these factors to improve patient care since traditional vital signs (macrohemodynamic) may not reflect early hypovolemia or tissue hypoperfusion.<sup>8</sup>

Most of the studies performed so far are from the hospital setting and focused their efforts initially on simple hemodynamic data such as heart rate (HR) or blood pressure (BP), both used in the Revised Trauma Score<sup>9</sup> (RTS) or the blood loss estimation of the American College of Surgeons<sup>10</sup> (ACS) Advanced Trauma Life Support (ATLS) classification of hemorrhagic shock and later on, analytical data obtained in the hospital, mainly lactate and base excess (BE).<sup>11-13</sup>

For this reason, we designed this study to analyze the diagnostic and prognostic possibilities of metabolic parameters in the first moments of care at the scene and to assess which determinations can constitute a decision-making tool both for therapeutic and prognostic purposes in aspects such as the destination of the patient and the activation of the diagnostic and therapeutic means that we must implement at the hospital level.

## Methods

### *Study design and setting*

An observational multicenter study conducted through a prospectively developed database of all trauma patients transferred as Trauma Code by SAMUR-Protección Civil to the four trauma centers in Madrid with which it maintains this code, during the years 2016-2019. Patients with isolated traumatic brain injury (TBI) were excluded.

The scope of action of the service is the public spaces of the city of Madrid, with 3.2 million inhabitants plus a million people per day of floating population, where they perform about 140 000 assistances per year. Since 2010, SAMUR-Protección Civil and the 4 trauma units have maintained a joint assistance procedure called the Trauma Code for victims of major trauma.<sup>14</sup> In this procedure, the emergency service attends all these patients with 2 physicians and 2 nurses on the scene.

According to this procedure, in all patients, a venous blood sample was taken at first vascular access (within 90 seconds) and analyzed at the scene using the point-of-care EPOC<sup>®</sup> device (Epocal Inc., Ottawa, Canada). This is a portable device that uses the same “platinum electrode” technology as the usual laboratories through cards containing microprocessor chips integrated with analyte samples. It provides in 3 minutes and 30 seconds, through a small venous or arterial sample (0.5 ml), the gasometric values, and some biochemical and hemacytometric values. The initial analytical results (pH, pCO<sub>2</sub>, HCO<sub>3</sub><sup>-</sup>, EB, hemoglobin, glycemia, creatinine, hematocrit, Na<sup>+</sup>, K<sup>+</sup>, Ca<sup>2+</sup>, Cl<sup>-</sup> and lactate), before the administration of any drug or fluid, were analyzed as independent variables in this study.

Injury assessment of patients was performed in the hospital setting using the New Injury Severity Score (NISS)<sup>15</sup> at least 24 hours after admission.

### *Statistical analysis*

The primary outcome of the study is the initial prognostic value that each metabolic parameter has on the injury severity or mortality of trauma patients susceptible to hemorrhagic shock due to trauma. We discarded patients with TBI as the only injury from the study.

We considered the NISS scores of each patient as dependent variables and the mortality variable. We determined the area under the curve (AUC) of the quantitative variables for four severity levels according to the NISS score (34-41, 42-49, 50-59, and > 60) and for mortality, and we obtained optimal cutoff points using the Youden index. Positive predictive value (PPV), and we calculated the negative predictive value (NPV) for these cutoff points. Given the large number of comparisons made in the study, there is the possibility of occasional isolated statistical significance, so we applied the Bonferroni method to adjust the p-value for each inde-

pendent variable according to the number of comparisons made.

We performed the descriptive analysis of the epidemiological variables (age, gender, mechanism of injury, ruling disease or days in intensive care) with indices of central tendency and dispersion (mean and standard deviation - SD) and percentage. Values of  $P < .05$  were considered significant. We performed statistical processing with the SPSS statistical package, version 18 (SPSS Inc., Chicago, IL, USA).

The research study was approved by our reference Ethics Committee (CEIC, Spanish Acronym, of the Hospital Clínico San Carlos de Madrid).

## Results

During the study period, 1039 trauma patients were included in the continuous emergency department registry (Figure 1). Patients were followed up during their hospital stay until discharge or death. Ninety-seven patients were discarded due to a lack of complete data, either in the out-of-hospital or in-hospital setting. The 233 patients presenting an isolated TBI without other pathology susceptible to bleeding were excluded. A total of 709 patients were included in the study.

The epidemiological characteristics of the population are like those of most studies of trauma patients (Table 1): mean age of 40.4 (SD 17.3) years and 77.6% male. The primary injury mechanisms were motorcycle accidents (21%), followed by high-altitude precipitation (19.2%), stab wounds (16.9%), and run-over (16.8%). Regarding mortality, 86 patients (12.1%) died during the first 30 days, with a significant difference between men (10.6%) and women (18.3%,  $P < .001$ ). Mean

baseline vital signs and analytical parameters are shown in Table 1.

The mean response time (time of arrival at the scene from the alert call) was 9 minutes and 2 seconds. The mean attendance time, which includes time on scene and transfers to the hospital, was 46 minutes and 26 seconds.

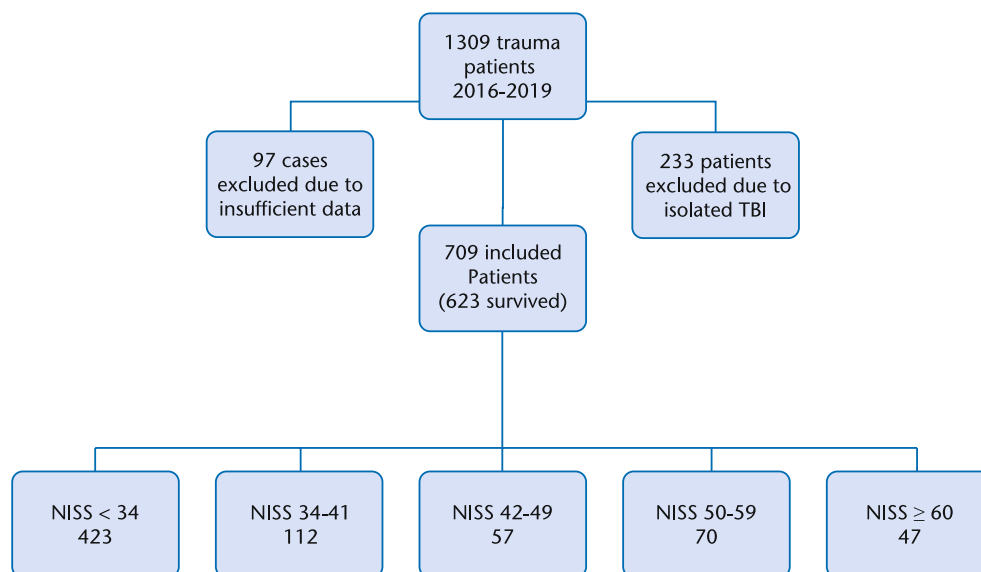
The analysis of the area under the receiver operating characteristic curve (AUC-ROC) of each parameter for each severity level is shown in Tables 2 and 3. For most NISS levels and values associated with metabolic parameters, with few exceptions, statistical significance ( $P < .05$ ) is observed, with a significant number of cases where the alternative hypothesis has a much higher probability ( $P < .001$ ). BE was significant for the highest severity level but not for mortality. The AUC-ROC for pH was 0.667, 0.668, 0.744, 0.758, and 0.70, with  $P < .0001$  for NISS of 34-41, 42-49, 50-59,  $\geq 60$ , and mortality. The NPVs were 62.1, 60.2, 68.3, 72, and 62.5, respectively, in all cases with  $P < .001$ .

PCO<sub>2</sub>, hemoglobin, and glycemia were the following parameters with the best PPV and NPV for all severity levels, also with  $P < .001$ .

Of the non-metabolic parameters, only GCS showed superior results to the analytical parameters, while SBP and RF maintained much lower values.

## Discussion

An out-of-hospital emergency medical service performed this study with short response times and through the assessment of metabolic parameters of a venous blood sample obtained at the time of cannulation of the first vascular access. Therefore, the context is different from that of most emergency departments.



**Figure 1.** Patient file, exclusion criteria and NISS and mortality outcome of the total number of patients included in the study.

NISS: New Injury Severity Score; TBI: traumatic brain injury.

**Table 1.** Descriptive characteristics of the study population

	N = 709 n (%)
<b>Age (years) [Mean (SD)]</b>	40 (17)
<b>Gender</b>	
Male	550 (77.6)
Female	159 (22.4)
<b>Injury mechanism</b>	
Car accident	65 (9.2)
Motorcycle accident	149 (21.0)
Cycling accident	13 (0.8)
Run over by a motor vehicle	119 (16.8)
Fall from height	136 (19.2)
Rollover	5 (0.7)
Fall to ground level	24 (3.4)
Knife/stab injury	120 (16.9)
Injury by firearm	9 (1.3)
Blunt force injury	10 (1.8)
Burn/explosion	29 (4.1)
Burial	6 (0.8)
Electrocution	2 (0.3)
Airplane accident	1 (0.1)
<b>Severity (points) [Mean (SD)]</b>	
ISS	24.19 (16.95)
NISS	28.77 (18.93)
<b>ICU stay [Mean (SD)]</b>	7.97 (13.84)
<b>Mortality at 30 days [n (%)]</b>	
Yes	86 (12.2)
No	621 (87.8)
<b>Analytical parameters [Mean (SD)]</b>	
pH	7.30 (0.13)
pCO <sub>2</sub> (mmHg)	47 (15)
HCO <sub>3</sub> (mmol/L)	23 (5)
Lactate (mmol/L)	4.7 (3.2)
BE (mmol/L)	-2.96 (5.08)
Na (mmol/L)	141 (4)
K (mmol/L)	3.78 (0.65)
Cl (mmol/L)	108 (4)
Ca (mmol/L)	1.2 (0.2)
Glu (mg/dL)	145 (50)
Hb (g/dL)	15.3 (2.1)
Hct (%)	45 (6)
Cr (mg/dl)	1.16 (0.47)
<b>Clinical parameters [Mean (SD)]</b>	
SBP (mmHg)	119 (31)
HR (bpm)	98 (26)
RR (brpm)	17 (6)
SpO <sub>2</sub> (%)	86 (25)
GCS (points)	12 (4)

ISS: Injury Severity Score; NISS: New Injury Severity Score; BE: base excess; Glu: blood glucose; Hb: hemoglobin; Hct: hematocrit; Cr: creatinine; SBP: systolic blood pressure; HR: heart rate; RR: respiratory rate; GCS: Glasgow Coma Scale.

The results may differ from other published studies due to the early extraction of this sample and its lack of treatment-related effects.

In our study, using different cutoff values for NISS, in all cases, it is observed that the most severe patients, according to this scale, have lower pH and higher PCO<sub>2</sub>, lactate, and BE results. The predictive capacity of each value independently is limited, but a combination of them could be clinically relevant together with other exploratory findings. In comparison with previous stud-

ies, it is striking that, in isolation, the base deficit could not predict higher mortality.

From the statistical point of view, the values with the most significant predictive capacity for severity are not lactate or BE but rather pH, PCO<sub>2</sub>, and glycemia. Our group<sup>16</sup> also described these data and other investigators<sup>17,18</sup> in patients attended for out-of-hospital cardiac arrest likely due to their greater sensitivity to tissue hypoxia and metabolic stress. However, this does not contradict what was shown by the ROC group,<sup>11</sup> also using blood analysis at the scene, who demonstrated that the use of lactacidemia improved the classifying capacity of the classic ACS criteria.

Along the same lines, the German trauma registry group<sup>19,20</sup> described the ability of lactate and BE measured early in the hospital (emergency department and intensive care) to predict mortality, length of stay or massive transfusion requirements. In fact, this same group has questioned the classic classification with exploratory data; thus, with a sample of more than 36 500 patients from the Trauma Register DGU,<sup>21</sup> they concluded that less than 10% were adequately classified according to the ATLS classification, while BE did have the capacity to predict transfusion requirements and mortality.<sup>22</sup> These same data have been confirmed by other groups, who have highlighted the predictive capacity of BE even in patients without alterations in their vital signs or in certain age ranges in which these are less altered, such as elderly patients. The existence of increased BE has also been correlated with the finding of free intra-abdominal fluid by eco FAST.<sup>23</sup>

Not only BE, but also lactate, have predictive ability for transfusion requirements, including hemodynamically stable patients, over and above the predictive ability of vital signs such as SBP.<sup>24</sup>

Importantly, the predictive ability of metabolic values is superior to that of classical hemodynamic values. In this study, pH and PCO<sub>2</sub> values probably have the greatest clinical usefulness, not only because of their statistical significance but also because they have optimal cut-off points that are farther from normal.

With respect to glycemia,<sup>25</sup> several studies in the last decade have confirmed it as a marker of severity, with different cut-off points depending on the studies.

The findings on hemoglobin and hematocrit deserve comment. Although their values are lower in more severe patients, the figures are not clinically relevant, undoubtedly due to the early arrival of the team (a response time of less than 10 minutes) and the taking of the sample, as evidenced by the fact that the optimal cut-off points in the ROC curve are 15.5 g/dL for hemoglobin and 44.5% for hematocrit.

The study presents a mortality distribution similar to that of other published studies of trauma patients,<sup>26</sup> with a higher mortality in the female subgroup, a fact about which different theories have been developed.<sup>27</sup>

These results support and reinforce the use of blood analysis at the scene as a means of estimating severity and alerting hospital services. As in cardiac arrest, very early metabolic values are of prognostic value.<sup>16,17</sup>

**Table 2.** Analytical parameters measured at the scene and their correlation with a NISS score equal to or greater than 34, 42, 50, 50, 60 and 30-day mortality

	NISS 34 ( $\geq 34$ points)				NISS 42 ( $\geq 42$ points)				NISS 50 ( $\geq 50$ points)				NISS 60 ( $\geq 60$ points)				30-day mortality			
	OPC	AUC	PPV (%)	NPV (%)	P	OPC	AUC	PPV (%)	NPV (%)	P	OPC	AUC	PPV (%)	NPV (%)	P	OPC	AUC	PPV (%)	NPV (%)	P
pH	7.315	0.667	61.23	62.11	<.001	7.315	0.668	64.1	60.2	<.001	7.295	0.744	70.7	68.3	<.001	7.275	0.758	62.2	72	<.001
pCO <sub>2</sub> (mmHg)	45.15	0.644	59.9	58.5	<.001	46.05	0.652	59.3	58.7	<.001	49.25	0.698	65.3	66.5	<.001	50.15	0.704	66.7	66.4	<.001
HCO <sub>3</sub> (mmol/L)	0.479					0.500					0.488						0.539			
Lactate (mmol/L)	4.055	0.556	36.5	71.6	.083	4.26	0.554	54.5	53.3	.151	4.425	0.615	58.7	59	.013	4.67	0.646	57.8	62.9	.007
EB (mmol/L)	-2.215	0.566	54.6	53.1	.313	-2.35	0.556	56.2	54.2	.302	-2.65	0.600	56	56.6	.236	-3.05	0.596	60	60.7	.038
Na (mmol/L)	0.502					0.507					0.520						0.487			
K (mmol/L)	3.75	0.597	53.3	57.1	.024	3.75	0.600	54.5	56.5	.048	3.75	0.592	54.7	54.2	.435		0.577			
Cl (mmol/L)	107.5	0.550	36.7	72.2	.033	107.5	0.557	61.7	51	.010		0.572					0.539			
Ca (mmol/L)	0.687					0.502					0.471						0.529			
Glu (mg/dL)	137.5	0.618	59.9	61.1	<.001	137.5	0.609	60.5	58.7	<.001	139.5	0.615	60	58.5	.020	141.5	0.616	60	60.9	.047
Hb (g/dL)	15.6	0.602	55.9	55.3	.0213	15.5	0.619	58.7	56.3	.004	15.2	0.617	60	59.5	.006	14.9	0.648	62.2	64.4	.001
Hct (%)	45.3	0.590	53.3	57.1	.048	43.5	0.607	47.9	68	<.001	45.3	0.597	58.7	5	.046	44.5	0.633	60	59.2	.002
Cr (mg/dl)	1.135	0.596	38	73.6	.006		0.552				1.15	0.575	56	52	.062		0.557			

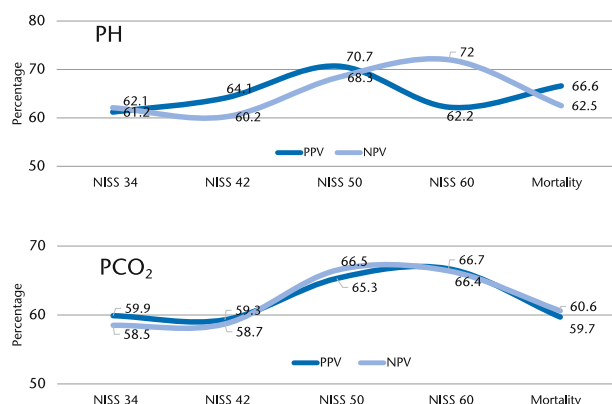
NISS: New Injury Severity Score; AUC: area under the curve; PPV: positive predictive value; NPV: negative predictive value; BE: base excess; BGLu: blood glucose; Hb: hemoglobin; OCO: optimal cutoff point; Hct: hematocrit; Cr: creatinine; Hb: hemoglobin; Hct, hematocrit.

**Table 3.** Clinical parameters measured at the scene and their correlation with a NISS score equal to or greater than 34, 42, 50, 60 and 30-day mortality

	NISS 34 ( $\geq 34$ points)				NISS 42 ( $\geq 42$ points)				NISS 50 ( $\geq 50$ points)				NISS 60 ( $\geq 60$ points)				30-day mortality			
	OPC	AUC	PPV (%)	NPV (%)	P	OPC	AUC	PPV (%)	NPV (%)	P	OPC	AUC	PPV (%)	NPV (%)	P	OPC	AUC	PPV (%)	NPV (%)	P
SBP (mmHg)	116.5	0.602	54.2	59.8	<.001	119.5	0.597	53.9	3.3	<.001	115.5	0.676	54.7	56.9	<.001	110.5	0.654	51.1	59.2	<.001
HR (bpm)	99.6	0.558	54.6	54.1	.022		0.549					0.550				104.5	0.612	51.1	60.6	<.001
RR (bpm)	16.5	0.601	37.9	42.5	.054	16.5	0.614	36.5	43.6	.086	16.5	0.592	54.7	47	.179	15.5	0.593	44.4	61.2	.067
SpO <sub>2</sub> (%)		0.553				95.5	0.557	59.9	54.2	.003	94.5	0.580	56	59.6	<.001	94.5	0.603	57.8	64.1	.002
GCS (points)	14.5	0.737	67.4	71.6	<.001	14.5	0.753	71.3	68.4	<.001	13.5	0.756	72	72.2	<.001	12.5	0.747	68.2	72.2	<.001

NISS: New Injury Severity Score; OPC: optimal cut-off point; AUC: area under the curve; PPV: positive predictive value; NPV: negative predictive value; SBP: systolic blood pressure; HR: heart rate; RR: respiratory rate; RF: respiratory frequency; GCS: Glasgow Coma Scale.





**Figure 2.** Positive and negative predictive values of pH and pCO<sub>2</sub>. NISS scores equal to or greater than 34, 42, 50 and 60 for mortality (cut-off values for pH and pCO<sub>2</sub> for each case are shown in Table 2).

NISS: New Injury Severity Score; PPV: positive predictive value; NPV: negative predictive value.

The main strengths of this work lie in the participation of four trauma units from four different hospitals together with the out-of-hospital emergency department, the presence of an on-site blood analyzer in all the advanced life support (ALS) units of the department, and the use of standardized severe trauma care protocols, so that all patients are treated homogeneously.

However, it also has its limitations, biases, and weaknesses. Our emergency service is unique in that it guarantees the presence of a second physician and a second nurse on site in serious cases that are transferred to the hospital with advance notice. The response times of our service, located in a large city with a high population density and no rural areas, are shorter than in other areas, which also results in higher survival rates in situations such as cardiac arrest. The performance of multiple statistical analyses with different cut-off points could increase the probability of finding significant results in some of them, although there are no relevant differences depending on the cut-off point used.

As conclusions, with all the caution that an observational study demands, we can say, in view of the homogeneous statistical significance offered by this study, that certain metabolic parameters analyzed early at the scene of the trauma itself can constitute an additional tool in the process of identifying the most serious patients. This will make it possible to make more accurate decisions both in the therapeutic aspect and in the transfer to the most useful unit for each patient.

**Conflict of Interests Disclosure:** None reported.

**Funding/Support:** The authors declare the non-existence of funding in relation to the present article.

**Ethical responsibilities:** All authors have confirmed the maintenance of confidentiality and respect for patient rights in the document of author responsibilities, publication agreement and assignment of rights to EMERGENCIAS. The study was approved by the Clinical Research Ethics Committee of the Hospital Clínico San Carlos de Madrid.

**Article not commissioned by the Editorial Committee and with external peer review.**

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