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Physiological parameters for Prognosis in Abdominal Sepsis (PIPAS) Study: a WSES observational study

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Abstract

Background: Timing and adequacy of peritoneal source control are the most important pillars in the management of patients with acute peritonitis. Therefore, early prognostic evaluation of acute peritonitis is paramount to assess the severity and establish a prompt and appropriate treatment. The objectives of this study were to identify clinical and laboratory predictors for in-hospital mortality in patients with acute peritonitis and to develop a warning score system, based on easily recognizable and assessable variables, globally accepted.

Methods: This worldwide multicentre observational study included 153 surgical departments across 56 countries over a 4-month study period between February 1, 2018, and May 31, 2018.

Results: A total of 3137 patients were included, with 1815 (57.9%) men and 1322 (42.1%) women, with a median age of 47 years (interquartile range [IQR] 28–66). The overall in-hospital mortality rate was 8.9%, with a median length of stay of 6 days (IQR 4–10). Using multivariable logistic regression, independent variables associated with in-hospital mortality were identified: age > 80 years, malignancy, severe cardiovascular disease, severe chronic kidney disease, respiratory rate ≥ 22 breaths/min, systolic blood pressure < 100 mmHg, AVPU responsiveness scale (voice and unresponsive), blood oxygen saturation level (SpO_2) < 90% in air, platelet count < 50,000 cells/mm3, and lactate > 4 mmol/l. These variables were used to create the PIPAS Severity Score, a bedside early warning score for patients with acute peritonitis. The overall mortality was 2.9% for patients who had scores of 0–1, 22.7% for those who had scores of 2–3, 46.8% for those who had scores of 4–5, and 86.7% for those who have scores of 7–8.

Conclusions: The simple PIPAS Severity Score can be used on a global level and can help clinicians to identify patients at high risk for treatment failure and mortality.

Keywords: Acute peritonitis, Source control, Early warning score, Emergency surgery

Introduction

Peritonitis is an inflammation of the peritoneum. Depending on the underlying pathology, it can be infectious or sterile [1]. Infectious peritonitis is classified into primary peritonitis, secondary peritonitis, and tertiary peritonitis. Primary peritonitis is a diffuse bacterial infection (usually caused by a single organism) without loss of integrity of the gastrointestinal tract, typically seen in cirrhotic patients with ascites or in patients with a peritoneal dialysis catheter. It has a low incidence in surgical wards and is usually managed without any surgical intervention. Secondary peritonitis is an acute peritoneal infection resulting from loss of integrity of the gastrointestinal tract. Tertiary peritonitis is a recurrent infection of the peritoneal cavity that occurs > 48 h after apparently successful and adequate surgical source control of secondary peritonitis. Secondary peritonitis is the most common form of peritonitis. It is caused by perforation of the gastrointestinal tract (e.g. perforated duodenal ulcer) by direct invasion from infected intra-abdominal viscera (e.g. gangrenous appendicitis). It is an important cause of patient morbidity and is frequently associated with significant morbidity and mortality rates [2], despite development in diagnosis and management.

Timing and adequacy of peritoneal source control are the most important pillars in the management of patients with acute peritonitis, being determinant to control or interrupt the septic process [2, 3].

Many peritonitis-specific scoring systems have been designed and used to grade the severity of acute peritonitis [4–7].

Patients with acute peritonitis are generally classified into low risk and high risk. "High risk" is generally intended to describe patients at high risk for treatment failure and mortality [6]. In high-risk patients, the increased mortality associated with inappropriate management cannot be reversed by subsequent modifications. Therefore, early prognostic evaluation of acute peritonitis is important to assess the severity and decide the aggressiveness of treatment. Moreover, in emergency departments of limited-resource hospitals, diagnosis of acute peritonitis is mainly clinical, and supported only by basic laboratory tests [8], making some scoring systems impractical to a large part of the world's population.

The objectives of this study were (a) to identify all clinical and laboratory predictors for in-hospital mortality in patients with acute peritonitis and (b) to develop a warning score system, based on easily recognizable and assessable variables, globally accepted, so as to provide the clinician with a simple tool to identify patients at high risk for treatment failure and mortality.

Methods

Study population

This worldwide multicentre observational study was performed across 153 surgical departments from 56

countries over a 4-month study period (February 1, 2018 – May 31, 2018). All consecutive patients admitted to surgical departments with a clinical diagnosis of acute peritonitis were included in the study. The following data were collected: age and gender; presence of comorbidities, namely primary or secondary immunodeficiency (chronic treatment with glucocorticoids, with immunosuppressive agents or chemotherapy, and patients with lymphatic diseases or with virus-related immunosuppression; solid or haematopoietic and lymphoid malignancy; severe cardiovascular disease (medical history of ischemic heart disease, history of heart failure, severe valvular disease [9]); diabetes with or without organ dysfunction; severe chronic kidney disease; and severe chronic obstructive pulmonary disease (COPD) [10]. Clinical findings were recorded at admission: abdominal findings (localized or diffuse abdominal pain, localized or diffuse abdominal rigidity); core temperature (defining fever as core temperature > 38.0 °C, and hypothermia as core temperature < 36.0 °C); heart rate (bpm); respiratory rate (breaths/min); systolic blood pressure (mmHg); alert/verbal/painful/unresponsive (AVPU) responsiveness scale [11]; and numerical rating scale (NRS) [12].

The following laboratory findings were also collected: blood oxygen saturation level (SpO_2) (%) in air, white blood count (WBC) (cells/mm^3), platelet count (cells/ mm^3), international normalised ratio (INR), C-reactive protein (CRP) (mg/l), procalcitonin (ng/ml), and lactate (mmol/l). Quick Sequential Organ Failure Assessment (qSOFA) score upon admission was calculated [13]. The modality and setting of acquisition of radiological investigations (abdominal x-ray, ultrasound [US], computer tomography [CT] scan) was specified. Peritonitis was classified as community-acquired or healthcare-acquired. Peritonitis was considered healthcare-associated in patients hospitalized for at least 48 h during the previous 90 days; or those residing in skilled nursing or long-term care facility during the previous 30 days; or those who have received intravenous therapy, wound care, or renal replacement therapy within the preceding 30 days. Source of infection, extent of peritonitis (generalized or localized peritonitis/abscess), source control (conservative treatment, operative or non-operative interventional procedures), and its adequacy were noted. The adequacy of the intervention was defined by the establishment of the cause of peritonitis and the ability to control the source of the peritonitis [14]. Delay in the initial intervention (> 24 h of admission), and adequacy of antimicrobial therapy (if guided by antibiograms performed) were assessed. Reoperation during the hospital stay, re-laparotomy strategy (open abdomen, planned re-laparotomy, on demand re-laparotomy) and its timing, immediate (within 72 h) infectious post-operative complications, delayed infectious post-operative complications, length of hospital stay (LOS), and in-hospital mortality were determined. All patients were monitored until they were discharged or transferred to another facility.

Study design

The centre coordinator of each participating medical institution collected data in an online case report database. Differences in local surgical practice of each centre were respected, and no changes were impinged on local management strategies. Each centre followed its own ethical standards and local rules. The study was monitored by a coordinating centre, which processed and verified any missing or unclear data submitted to the central database. The study did not attempt to change or modify the clinical practice of the participating physicians. Accordingly, informed consent was not needed and each hospital followed their ethical rules for formal research including an ethical approval if approval was needed. The data were completely anonymised. The study protocol was approved by the board of the World Society of Emergency Surgery (WSES), and the study was conducted under its supervision. The board of the WSES granted the proper ethical conduct of the study. The study met and conformed to the standards outlined in the Declaration of Helsinki and Good Epidemiological Practices.

Statistical analysis

The data were analysed in absolute frequency and percentage, in the case of qualitative variables. Quantitative variables were analysed as medians and interquartile range (IQR). Univariate analyses were performed to study the association between risk factors and in-hospital mortality using a chi-square test, or a Fisher's exact test, if the expected value of a cell was < 5. All tests were two-sided, and p values of 0.05 were considered statistically significant.

To identify independent risk factors associated with in-hospital mortality, a multivariable logistic regression analysis was performed selecting independent variables that had p value < 0.05 in the univariate analysis. Then, a backward selection method was applied to select a limited number of variables, using a likelihood ratio test for comparing the nested models ($\alpha = 0.05$). At each step, we removed from the previous model the variable with the highest p value greater than α, checking the fit of the obtained model, and then stopping when all p values were less than α. Then, we checked the global performance of the test calculating the area under the receiver operating characteristic (ROC) curve. All statistical analyses were performed using the Stata 11 software package (StataCorp, College Station, TX).

Results

Patients and diagnosis

During the study, 3137 patients from 153 hospitals worldwide were collected; these included 1815 (57.9%)

men and 1322 (42.1%) women, with a median age of 47 years (IQR, 28–66). Considering World Health Organization regions, 1981 (63.1%) patients were collected in countries belonging to European region, 396 (12.6%) patients were from the African region, 275 (8.8%) from the region of the Americas, 239 (7.6%) from the South-East Asia region, 173 (5.5%) from the Eastern-Mediterranean region, and 73 (2.3%) from the Western Pacific region.

Forty-one (1.3%) patients were asymptomatic, while 990 (31.6%) reported localized abdominal pain, 665 (21.2%) localized abdominal rigidity, 797 (25.4%) diffuse abdominal pain, and 592 (18.9%) diffuse abdominal rigidity. In 52 (1.7%) patients, abdominal findings were not reported. Three hundred and thirty (10.5%) patients underwent abdominal x-ray, 756 (24.1%) patients had an US, 1016 (32.4%) abdominal CT scan, 189 (6.0%) patients had both abdominal x-ray and US, 76 (2.4%) had both abdominal x-ray scan and CT, 199 (6.3%) patients had both CT scan and US, 93 (3.0%) patients underwent abdominal x-ray scan, US and CT, and 445 (14.3%) patient did not undergo any radiological investigation. In 33 (1.1%) patients, radiological diagnosis was not specified.

Considering the setting of acquisition, 2826 (90.1%) patients were affected by community-acquired intra-abdominal infections (IAIs), while the remaining 311 (9.9%) suffered from healthcare-associated IAIs; moreover, 1242 patients (39.6%) were affected by generalized peritonitis, while 1895 (60.4%) suffered from localized peritonitis or abscesses. The cause of infection was acute appendicitis in 1321 (42.1%) patients, acute cholecystitis in 415 (13.2%), gastroduodenal perforation in 364 (11.6%) patients, small bowel perforation in 219 (7.0%), acute diverticulitis in 217 (6.9%), colonic perforation in 203 (6.5%), post-traumatic perforation in 79 (2.5%), acute infected pancreatitis in 40 (1.3%), pelvic inflammatory disease (PID) in 30 (1.0%), and other causes in 249 (7.9%).

Management

Among all patients enrolled in the PIPAS Study, 377 (12%) underwent non-operative procedures, and the other 2760 (88.0%) patients underwent operative interventional procedures as first-line treatment. Source control was considered inadequate in 247 (247/2834, 8.7%) patients who underwent surgical procedures. In 1630 (1630/2834, 57.5%) patients the initial intervention was delayed. Among 2159 patients who received antimicrobial therapy, in 336 (15.6%), it was considered inadequate. During the same hospitalization, 242 (242/2760, 8.8%) patients underwent a second procedure after 4 (IQR 2–7) days because of a postoperative complication or a worsening of the initial stage. In particular, 79 (2.9%) patients underwent an open abdomen surgery, 57 (2.1%) a planned relaparotomy, and 87 (3.2%) an on-demand relaparotomy, and in 19 (0.7%) patients, no specific procedure was specified.

Immediate post-operative complications were observed in 339 (339/2760, 12.3%) patients who underwent a surgical procedure; among them we observed ongoing peritonitis in 174 (6.3%) patients, multi-organ failure in 33 (1.2%), bleeding in 32 (1.2%), cardiovascular complications in 17 (0.6%), respiratory complications in 15 (0.5%), sepsis or septic shock in 13 (0.5%), and other complications in 55 (2.0%). Delayed post-operative complications were detected in 774 (774/2760, 28.0%) patients who underwent an interventional procedure; in particular, they suffered from surgical site infections in 343 (12.4%) patients, post-operative peritonitis in 132 (4.8%), post-operative abdominal abscess in 118 (4.3%), respiratory complications in 54 (2.0%),cardiovascular complications in 39 (1.4%), sepsis or septic shock in 33 (1.2%), ileus in 22 (0.8%), multi-organ failure in 18 (0.7%), renal complications in 13 (0.5%), and other complications in 79 (2.9%).

Outcome

The overall in-hospital mortality rate was 8.9%. The median duration of hospitalization was 6 days (IQR 4–10). Bivariate analyses were performed to analyse the association between risk factors and in-hospital mortality using a two-sided chi-square test or a two-sided Fisher's exact test where appropriate. Distribution of clinical predictive variables of in-hospital mortality is reported in Table 1. Distribution of laboratory predictive variables of in-hospital mortality is reported in Table 2.

Independent variables associated with in-hospital mortality according to the multivariable logistic regression are reported in Table 3. The model was highly significant ($p < 0.0001$), and the global performance of the test is explained by the area under the ROC curve, which is equals to 0.84 (95% CI).

Developing the severity score

The second aim of the study was to develop a severity score for patients with a clinical diagnosis of acute peritonitis that is simple and globally acceptable with a good prognostic value. Only the significant clinical variables associated with in-hospital mortality obtained from the multivariable logistic regression model were included, excluding the lactate, and platelet count. This modification was done for three reasons: (a) to simplify the score, (b) to make it more universal and globally acceptable, and (c) because of lack of facilities to obtain lactate in low-income countries. The coefficients of the variables were used to develop the score, and not the Odds Ratio. The significant clinical variables were subjected to different direct logistic regression models using either simple binomial variables or ordinal data, to arrive at a

Table 1 Distribution of clinical predictive variables of in-hospital mortality

Variables	Total patients	Dead	Survivors	RR	*p* value
	n 3137	*n* 280	*n* 2857		
	(100%)	(8.9%)	(91.1%)		
Age > 80 years	246 (7.8)	72 (25.7)	174 (6.1)	4.07 (3.22–5.14)	< 0.001
Immunodeficiency	240 (7.7)	56 (20.0)	184 (6.4)	3.02 (2.32–3.92)	< 0.001
Malignancy	333 (10.6)	83 (29.6)	250 (8.8)	3.55 (2.82–4.46)	< 0.001
Severe cardiovascular disease	406 (12.9)	106 (37.9)	300 (10.5)	4.10 (3.30–5.10)	< 0.001
Diabetes	400 (12.8)	76 (27.1)	324 (11.3)	2.55 (2.00–3.25)	< 0.001
Severe CKD	141 (4.5)	52 (18.6)	89 (3.1)	4.85 (3.78–6.22)	< 0.001
Severe COPD	186 (5.9)	60 (21.4)	126 (4.4)	4.33 (3.39–5.52)	< 0.001
Core temperature (°C)					
< 36.0	85 (2.7)	23 (8.2)	62 (2.2)	3.21 (2.22–4.64)	< 0.001
36.0–38.0	2292 (73.1)	185 (66.1)	2107 (73.7)	0.72 (0.57–0.91)	< 0.05
> 38.0	760 (24.2)	72 (25.7)	688 (24.1)	1.08 (0.84–1.40)	0.54
Hearth rate (bpm)					
< 60	8 (0.3)	1 (0.4)	7 (0.2)	1.40 (0.22–8.80)	0.72
60–100	1919 (61.2)	117 (41.8)	1802 (63.1)	0.46 (0.36–0.57)	< 0.001
> 100	1210 (38.6)	162 (57.9)	1048 (36.7)	2.19 (1.74–2.74)	< 0.001
Systolic blood pressure (mmHg)					
< 90	138 (4.4)	49 (17.5)	89 (3.1)	4.61 (3.57–5.96)	< 0.001
90–100	388 (12.4)	70 (25.0)	318 (11.1)	2.36 (1.84–3.03)	< 0.001
> 100	2610 (83.2)	161 (57.5)	2449 (85.7)	0.27 (0.22–0.34)	< 0.001
Respiratory rate (breaths/min)					
< 22	2244 (71.5)	124 (44.3)	2120 (74.2)	0.32 (0.25–0.40)	< 0.001
22–29	684 (21.8)	97 (34.6)	587 (20.5)	1.90 (1.50–2.39)	< 0.001
30–35	154 (4.9)	39 (13.9)	115 (4.0)	3.13 (2.33–4.21)	< 0.001
> 35	55 (1.8)	20 (7.1)	35 (1.2)	4.31 (2.98–6.23)	< 0.001
AVPU responsiveness scale					
Alert	2917 (93.0)	187 (66.8)	2730 (95.6)	0.15 (0.12–0.19)	< 0.001
Voice	123 (3.9)	54 (19.3)	69 (2.4)	5.85 (4.62–7.41)	< 0.001
Pain	74 (2.4)	23 (8.2)	51 (1.8)	3.70 (2.59–5.30)	< 0.001
Unresponsive	23 (0.7)	16 (5.7)	7 (0.2)	8.21 (6.12–11.01)	< 0.001
NRS					
0–3	80 (2.6)	16 (5.7)	64 (2.2)	2.32 (1.47–3.64)	< 0.001
4–6	1512 (48.2)	112 (40.0)	1400 (49.0)	0.72 (0.57–0.90)	< 0.05
7–10	1112 (35.4)	128 (45.7)	984 (34.4)	1.53 (1.23–1.92)	< 0.001
Not reported	433 (13.8)	24 (8.6)	409 (14.3)	NA	NA
qSOFA score					
0	1367 (43.6)	37 (13.2)	1330 (46.6)	0.20 (0.14–0.28)	< 0.001
1	1323 (42.2)	109 (38.9)	1214 (42.5)	0.87 (0.96–1.10)	0.25
2	353 (11.3)	84 (30.0)	269 (9.4)	3.38 (2.68–4.26)	< 0.001
3	94 (3.0)	50 (17.9)	44 (1.5)	7.04 (5.61–8.82)	< 0.001

All *p* values calculated using two-sided chi-square test

RR: risk ratio, *NA*: not applicable, *CKD*: chronic kidney disease, *COPD*: chronic obstructive pulmonary disease, *AVPU*: alert/verbal/painful/unresponsive, *NRS*: numerical rating scale, *qSOFA*: Quick Sequential Organ Failure Assessment

Table 2 Distribution of laboratory predictive variables of in-hospital mortality

Variables	Total patients	Dead	Survivors	RR	*p* value
	n 3137	*n* 280	*n* 2857		
	(100%)	(8.9%)	(91.1%)		
Blood oxygen saturation level (SpO_2) (%) in air					
> 92	2782 (88.7)	152 (54.3)	2630 (92.1)	0.15 (0.12–0.19)	< 0.001
90–91	198 (6.3)	66 (23.6)	132 (4.6)	4.58 (3.62–5.79)	< 0.001
85–89	99 (3.1)	41 (14.6)	58 (2.0)	5.26 (4.04–6.85)	< 0.001
< 85	21 (0.7)	9 (3.2)	12 (0.4)	4.93 (2.97–8.18)	< 0.001
Not reported	37 (1.2)	12 (4.3)	25 (0.9)	NA	NA
WBC (cells/mm^3)					
> 12,000	1950 (62.2)	182 (65.0)	1768 (61.9)	1.13 (0.89–1.43)	0.30
4000–12,000	1043 (33.2)	63 (22.5)	980 (34.3)	0.58 (0.44–0.76)	< 0.001
< 4000	94 (3.0)	29 (10.4)	65 (2.3)	3.74 (2.70–5.18)	< 0.001
Not reported	50 (1.6)	6 (2.1)	44 (1.5)	NA	NA
Platelet count (cells/ mm^3)					
> 150,000	2606 (83.1)	183 (65.4)	2423 (84.8)	0.38 (0.31–0.49)	< 0.001
50,000–1,500,000	387 (12.3)	73 (26.1)	314 (11.0)	2.51 (1.96–3.20)	< 0.001
< 50,000	32 (1.0)	18 (6.4)	14 (0.5)	6.67 (4.81–9.24)	< 0.001
Not reported	112 (3.6)	6 (2.1)	106 (3.7)	NA	NA
INR					
> 3	23 (0.7)	12 (4.3)	11 (0.4)	6.06 (4.03–9.11)	< 0.001
1.2–3	296 (9.4)	72 (25.7)	224 (7.8)	3.32 (2.61–4.22)	< 0.001
< 1.2	1954 (62.3)	149 (53.2)	1805 (63.2)	0.69 (0.55–0.86)	0.001
Not reported	864 (27.5)	47 (16.8)	817 (28.6)	NA	NA
CRP (mg/l)					
> 200	450 (14.3)	70 (25.0)	380 (13.3)	1.99 (1.55–2.56)	< 0.001
101–200	462 (14.7)	51 (18.2)	411 (14.4)	1.29 (0.97–1.72)	0.08
5–100	946 (30.2)	69 (24.6)	877 (30.7)	0.76 (0.58–0.98)	0.04
< 5	258 (8.2)	3 (1.1)	255 (8.9)	0.12 (0.04–0.37)	< 0.001
Not reported	1471 (46.9)	157 (56.1)	1314 (46.0)	NA	NA
Procalcitonin (ng/ml)					
> 10	85 (2.7)	31 (11.1)	54 (1.9)	4.47 (3.30–6.06)	< 0.001
0.5–10	260 (8.3)	42 (15.0)	218 (7.6)	1.96 (1.44–2.64)	< 0.001
< 0.5	100 (3.2)	3 (1.1)	97 (3.4)	0.33 (0.11–1.01)	0.03
Not reported	2692 (85.8)	204 (72.9)	2488 (87.1)	NA	NA
Lactate (mmol/l)					
>4	139 (4.4)	61 (21.8)	78 (2.7)	6.01 (4.79–7.54)	< 0.001
1–4	615 (19.6)	86 (30.7)	529 (18.5)	1.82 (1.43–2.31)	< 0.001
< 1	136 (4.3)	6 (2.1)	130 (4.6)	0.48 (0.22–1.07)	0.06
Not reported	2247 (71.6)	127 (45.4)	2120 (74.2)	NA	NA

All *p* values calculated using two-sided chi-square test
RR: risk ratio, *NA*: not applicable, *WBC*: white blood count, *INR*: international normalised ratio, *CRP*; C-reactive protein

simplified and acceptable model. Direct logistic regression model of the clinical variables affecting mortality which were used to develop the score is reported in Table 4. The score would have become complicated if we had to follow the model proposed by Moons et al. [15], whereby the coefficient would have to be multiplied by 10 and the value approximated to the nearest integral to get a score. This meant that the scores derived from

Table 3 Results of multinomial logistic regression for the analysis of variables associated with in-hospital mortality

Variables	OR	95% CI	*p* value
Age > 80 years	2.11	1.43–3.10	< 0.001
Malignancy	3.02	2.15–4.24	< 0.001
Severe cardiovascular disease	2.76	1.97–3.87	< 0.001
Severe chronic kidney disease	3.33	2.12–5.23	< 0.001
Respiratory rate ≥ 22 breaths/min	3.38	2.23–5.13	< 0.001
Systolic blood pressure < 100 mmHg	2.18	1.58–3.00	< 0.001
AVPU responsiveness scale voice or unresponsive	3.07	2.10–4.51	< 0.001
Blood oxygen saturation level (SpO_2) < 90% in air	2.67	1.64–4.32	< 0.001
Platelet count < 50,000 cells/ mm^3	4.81	2.07–11.20	< 0.001
Lactate > 4 mmol/l	4.00	2.58–6.23	< 0.001

CI: confidence interval, *OR*: odds ratio, *AVPU*: alert/verbal/painful/unresponsive

the model would be 10, 11, 9, 12, 8, 9, 9, and 14, making it very complex. Hence, it was decided to approximate the coefficient to the nearest integral number and test the model. Since the coefficients were approximated to 1, each of these variables could have a score of 1 or 0 with a maximum score of 8 and a range of 0–8. The simplified and finalized the PIPAS Severity Score is shown in the Appendix.

The PIPAS Severity Score had a very good ability of distinguishing those who survived from those who died (Fig. 1). The ROC curve showed that the best cutoff point for predicting mortality was a PIPAS Severity Score of 1.5 having a sensitivity of 74.3%, a specificity of 82.2% (Fig. 2) and an area under the curve of 85.1%. The overall mortality was 2.9% for the patients who had scores of 0 and 1, 22.7% for those who had scores of 2 and 3, 46.8% for those who had scores 4 and 5, and 86.7% for those who have scores 7–8.

Discussion

Using the multivariable logistic regression, ten independent variables associated with in-hospital mortality were identified. The model was highly significant, with a good global performance of the test. Excluding platelet count and lactate, eight bedside easy-to-measure parameters were recognized to develop an early warning score, the PIPAS Severity Score, assessing anamnestic data (age > 80 years, malignancy, severe cardiovascular disease, severe chronic kidney disease), and physiological functions (respiratory rate ≥ 22 breaths/min, systolic blood pressure < 100 mmHg, AVPU responsiveness scale voice or unresponsive, blood oxygen saturation level (SpO_2) < 90% in air).

The PIPAS Severity Score, taking into account physiological parameters recognizable on hospital admission, immediately allows clinicians to assess the severity and decide the aggressiveness of treatment. Particularly for clinicians working in low- and middle-income countries, where diagnostic imaging is often insufficient, and in some instances completely lacking, the utility of this score system is remarkable [16].

Sometimes, the atypical clinical presentation of acute peritonitis may be responsible for a delay in diagnosis and treatment. Therefore, a triage system that quickly recognizes patients at high risk for mortality and allows to

Table 4 Direct logistic regression model with clinical variables affecting mortality of patients used to develop the score

Variable	Estimate	SE	Wald test	*P*	OR	95% CI	
						LL	UL
Age > 80 years	0.97	0.19	25.91	< 0.0001	2.63	1.81	3.89
Malignancy	1.13	0.17	42.43	< 0.0001	3.11	2.21	4.37
Severe CVD	0.88	0.17	26.09	< 0.0001	2.41	1.72	3.38
Severe CKD	1.2	0.23	26.23	< 0.0001	3.32	2.1	5.26
RR ≥ 22 breaths/min	0.75	0.16	22.61	< 0.0001	2.11	1.55	2.87
SBP < 100 mmHg	0.86	0.17	27.29	< 0.0001	2.37	1.71	3.27
AVPU responsiveness scale: not completely alert.	1.35	0.2	47.98	< 0.0001	3.86	2.63	5.65
Blood oxygen saturation level: SpO_2 < 90% in air	0.87	0.25	12.15	< 0.0001	2.39	1.46	3.89
Constant	− 3.79	0.13	834.77	< 0.0001	0.023	–	–

SE: standard error, *OR*: odds ratio, *CI*: confidence interval, *LL*: lower limit, *UL*: upper limit, *CVD*: cardiovascular disease, *CKD*: chronic kidney disease, *RR*: respiratory rate, *SBP*: systolic blood pressure, *AVPU*: alert/verbal/painful/unresponsive

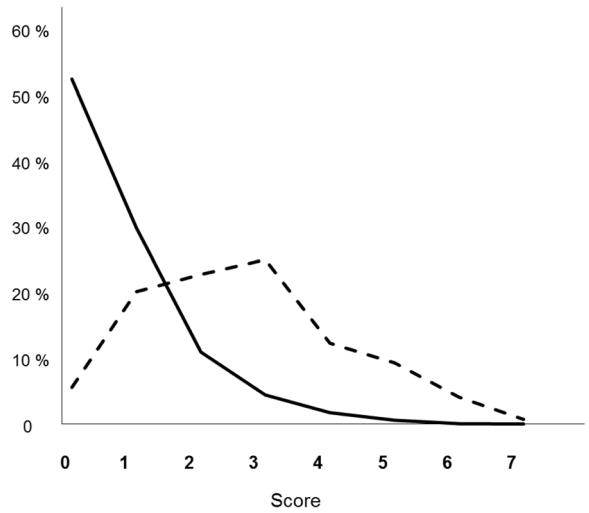

Fig. 1 Distribution of the percentile PIPAS Severity Score of hospitalized peritonitis patients for those who survived (*continuous line*) ($n = 2832$) and those who died (*interrupted line*) ($n = 268$). Global data from 153 worldwide surgical departments in 56 countries, over a 4-month study period (February 1, 2018–May 31, 2018). Thirty-seven patients (1.2%) had missing data in whom the score could not be computed

transfer them immediately to an acute care unit is a vital component of the emergency services. As a consequence, any process of improving the quality of emergency care globally should focus on simple diagnostic criteria based on physical examination findings that can recognize patients needing critical care. From a global perspective, a feasible, low-cost method of rapidly identifying patients requiring critical care is crucial. Early warning system scores utilize physiological, easy-to-measure parameters, assessing physiological parameters such as systolic blood pressure, pulse rate, respiratory rate, temperature, oxygen saturations, and level of consciousness [17].

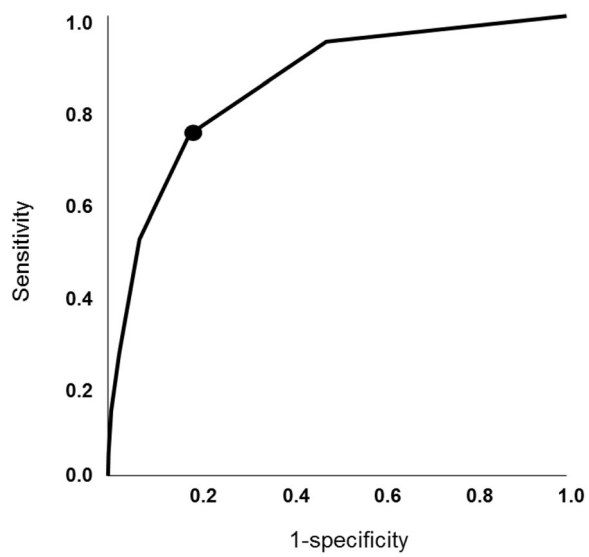

Fig. 2 Receiver operating characteristic (ROC) curve for the best PIPAS Severity Score (1.5, black circle) that predicted mortality in peritonitis patients. Global data from 153 worldwide surgical departments in 56 countries, over a 4-month study period (February 1, 2018–May 31, 2018)

The statistical analysis shows that the PIPAS Severity Score has a very good ability of distinguishing those who survived from those who died. The overall mortality was 2.9% for the patients who had scores of 0 and 1, 22.7% for those who had scores of 2 and 3, 46.8% for those who had scores of 4 and 5, and 86.7% for those who have scores of 7–8.

PIPAS Study has strengths and limitations. It is an observational multicentre study involving a large, but probably not representative, number of hospitals worldwide, since the majority of patients were collected in countries belonging to the WHO European region. Moreover, its validity needs to be tested in future large prospective series before potentially serving as a template for future database and research into patient outcomes. Finally, a potential limitation may be the high rate of patients with acute appendicitis enrolled in the study (42.1%). Some authors [18], after excluding patients with perforated appendicitis, found that the cure rate among patients who had peritonitis and were enrolled in clinical trials, was much higher than that of patients who were not enrolled and that the mortality rate was much lower. Although, delineating the source of infection as accurately as possible prior to surgery is described as the primary aim and the first step in managing acute peritonitis, in emergency departments of limited-resource hospitals, diagnosis of acute peritonitis is mainly clinical, and supported only by basic laboratory tests, and excluding acute appendicitis in the pre-operative phase would make the score impractical to a large part of the world's population.

Conclusions

This worldwide multicentre observational study was performed in 153 surgical departments from 56 countries over a 4-month study period (February 1, 2018–May 31, 2018). All consecutive patients admitted to surgical departments with clinical diagnosis of acute peritonitis were included in the study. The most significant independent variables associated with in-hospital mortality were adjusted to clinical criteria and were used to create a new bedside early warning score for patients with acute peritonitis. The simple PIPAS Severity Score for patients with acute peritonitis can be used on the global level and can help clinicians to assess patients with acute peritonitis at high risk for treatment failure and mortality. The authors created an acronym for the PIPAS Severity Score to help remember the variables "Scores Must Be Simple For Sepsis Risk Assessment" (severe cardiovascular disease, malignancy, blood oxygen saturation level, severe chronic kidney disease, fully alert, systolic blood pressure, respiratory rate, age).

Apenndix

Table 5 PIPAS Severity Score for patients with acute peritonitis (range 0–8)

Variables	Score
Age (years)	
80 or more	1
Less than 80	0
Malignancy	
Yes	1
No	0
Severe cardiovascular disease	
Yes	1
No	0
Severe chronic kidney disease	
Yes	1
No	0
Respiratory rate ≥ 22 breaths/min	
Yes	1
No	0
Systolic blood pressure < 100 mmHg	
Yes	1
No	0
Blood oxygen saturation level (SpO_2) < 90% in air	
Yes	1
No	0
AVPU responsiveness scale full alert	
No	1
Yes	0

Abbreviations

AVPU: Alert/verbal/painful/unresponsive; COPD: Chronic obstructive pulmonary disease; CRP: C-reactive protein; CT: Computer tomography; INR: International normalised ratio; IQR: Interquartile range; LOS: Length of hospital stay; NRS: Numerical rating scale; PID: Pelvic inflammatory disease. IAIs: intra-abdominal infections; qSOFA: Quick Sequential Organ Failure Assessment; ROC: Receiver operating characteristic; US: Ultrasound; WBC: White blood count; WSES: World Society of Emergency Surgery

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Authors' contributions

M Sartelli designed the study and wrote the manuscript. FM Abu-Zidan developed the severity score. FM Labricciosa performed the statistical analysis. All authors participated in the study. All authors read and approved the final manuscript.

Availability of data and materials

The authors are responsible for the data described in the manuscript and assure full availability of the study material upon request to the corresponding author.

Ethics approval and consent to participate

The data was completely anonymised, and no patient or hospital information was collected in the database. The study protocol was approved by the board of the WSES, and the study was conducted under its supervision. The board of the WSES granted the proper ethical conduct of the study.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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