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Research Paper

Are admission laboratory values in isolation meaningful for predicting surgical outcome in patients with perforated peptic ulcers?

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ABSTRACT

Background: The study aimed to calculate the predictive value of admission laboratory values in patients with perforated peptic ulcers.
Methods: A retrospective, cohort analytical, observational study was performed, including patients with surgically confirmed perforated peptic ulcers over a 5-year period. Demographic data and admission laboratory values were collected from hospital electronic databases. Outcomes measured were in-hospital mortality, intensive care unit (ICU) admission and length of stay. The significance of categorical variables was calculated by chi-square and Fisher's exact test. Logistic regression analysis was performed to determine univariately statistically significant variables.
Results: In total, 188 patients met the inclusion criteria. The median age was 46 (range 15–87) years with a male predominance of 71.3 % ($n = 134$). The median length of hospital stay was 7 (range 1–94) days and 31.4 % ($n = 59$) of patients were admitted to the ICU. Post-operative in-hospital mortality was 25.0 % ($n = 47$). Predicting the categorical outcome of in-hospital mortality, abnormal haemoglobin, platelet count, urea, creatinine and potassium levels were all found to be statistically significant in the univariate analysis. Age (odds ratio [OR] 1.03), haemoglobin (OR 4.36) and creatinine (OR 7.76) levels were significant in the multivariate analysis.
Conclusions: Mortality rate among patients with perforated peptic ulcer disease is still substantial. Admission laboratory values showed statistical significance as outcome indicators and were valuable to assist in predicting the prognosis. An abnormally high serum creatinine level was the strongest single predictor of both mortality and ICU admission.
Key message: Initial laboratory findings of patients admitted for perforated peptic ulcer showed that an abnormally high serum creatinine level was the strongest single predictor of both mortality and ICU admission.

Background

Annually, >4 million people are affected by peptic ulcer disease worldwide [1]. Peptic ulcer disease is complicated by bleeding, obstruction and perforation [2]. Bleeding is the most common complication, followed by perforation [3].

The incidence of perforation is 4–10 per 100,000 population per annum and can be the primary reason for the first hospital presentation in patients with peptic ulcer disease [4,5]. Endoscopic management and modern interventional radiology techniques have improved outcomes for bleeding ulcers, but outcomes for perforation have remained mostly unchanged [6,7]. Perforation is the cause of >70 % of deaths associated with peptic ulcer disease [8]. Sepsis and septic shock are common complications and frequently the ultimate cause of mortality [9–11]. Incongruent findings have been published reporting that perforated peptic ulcer carries a mortality rate ranging from 1.3 % to 40 % [2,3,7,9–21].

Admission status has been described as a significant prognostic indicator in patients with peptic ulcer perforation [13]. The diagnosis must be made early, resuscitation efforts initiated swiftly and rapid surgical intervention performed to improve patient outcome [12,22].

In a condition such as perforated peptic ulcer disease, electrolyte disturbances, anaemia, hypoalbuminaemia, renal failure and leucocytosis can all be considered as part of the sepsis syndrome [3]. The diagnosis of a perforated peptic ulcer cannot be made by using laboratory values in isolation and these values are non-specific [12]. Laboratory values, however, are good indicators of organ dysfunction and both local and

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systemic inflammation. These values are also used to exclude other pathologies, such as acute pancreatitis [8,18,22]. The major advantage of laboratory values in risk stratification is that they are objective in nature, routinely done and readily available [6].

Different scoring systems, summarised in Table 1, are used to provide an objective description of the patient's condition at a specific stage in the disease process. These scoring systems assist the physician with the diagnosis, give guidance regarding the course that the disease is taking in the specific patient and facilitate the surgeon's decision pertaining to the appropriate management and treatment algorithm [2]. These scoring systems use different subsets of available laboratory values in an attempt to predict mortality. Our question was whether admission laboratory findings were of any value in isolation, and if they could be used as a reliable indicator of prognosis.

The objective of the study was to calculate the predictive value in terms of surgical outcome (in-hospital mortality as well as intensive care unit [ICU] admission, length of stay in the ICU and the duration of hospitalisation) of different routine admission laboratory values in patients with perforated peptic ulcers.

Methods

A retrospective, cohort analytical, observational study was performed. All consecutive patients from July 2014 to June 2019 with surgically confirmed (during laparotomy) perforated peptic ulcer (gastric or duodenal) disease and available demographic and admission laboratory data were enrolled. Pelonomi Tertiary Hospital in Bloemfontein provides the bulk of the acute care surgical and trauma services for the Free State Province in South Africa.

The exclusion criteria were:

- histological confirmed malignant perforations;
- traumatic or iatrogenic perforations;
- perforations due to caustic ingestion or foreign bodies;
- patients managed conservatively without surgical intervention;
- patients who had surgery but no confirmation of a perforated ulcer; and
- patients younger than 13 years of age.

No laparoscopic surgery for peptic ulcer disease was performed during our study period. In-hospital mortality was defined as any death occurring during or after surgical intervention before discharge from hospital. ICU admission included days admitted to ICU at any stage after surgery.

Data were collected for all patients who met the inclusion criteria. Demographic data, which included the patient's age and biological sex, were collected from Pelonomi Hospital's electronic database (Meditech) and matched to the National Health Laboratory Service (NHLS) database (Labtrak). The University of the Free State (UFS) Department of Surgery statistical database and Pelonomi Hospital theatre record books were used to verify concordance of collected data.

The following laboratory values on admission were collected from the NHLS database (Labtrak):

- full blood count (haemoglobin level, haematocrit, white cell count, platelet count);
- renal function (urea and creatinine levels);
- electrolytes (sodium and potassium levels);
- inflammatory markers (C-reactive protein [CRP]); and
- albumin level.

The reference range for normal laboratory values used by the South African NHLS was applied to the laboratory findings, with values outside normal range categorised as abnormal low or abnormal high. Data captured were recorded on the data collection form and transferred into Microsoft Excel spreadsheet that served as a second copy of all data.

Data analysis was done by the Department of Biostatistics of the UFS using SAS Version 9.4 (SAS Institute Inc.; Cary, NC). Numerical variables were summarised by medians and interquartile ranges (IQR) due to skew distributions and categorical variables by frequencies and percentages. Skew distributions were identified using visual inspection of data distribution and outliers. Since both high and low laboratory values may be associated with poor outcomes, and there is thus not a linear increase in risk, laboratory values were categorised into low, normal and high. Chi-square and Fisher's exact tests were used to assess the significance of associations of categorical variables with categorical outcomes. Logistic regression analysis with backward elimination was performed using variables identified as statistically significant on univariate analyses. Risk was presented as an odds ratio (OR) with 95 % confidence interval (95 % CI). Calculation of sensitivity, specificity, positive and negative predictive values and area under the receiver operating characteristic (ROC) curve.

Table 1
Laboratory values that form part of scoring systems used for prediction models in patients with perforated peptic ulcers [2,23].

Scoring system used for outcome prediction	Target population	Outcome measured	Laboratory values used as part of scoring system
Hacettepe score [16]	Patients with perforated peptic ulcer	30-day mortality	Acute renal failure, white blood cell count
Jabalpur score [24]	Patients with perforated peptic ulcer	30-day mortality	Serum creatinine
PULP (peptic ulcer perforation) score [15]	Patients with perforated peptic ulcer	30-day mortality	Liver failure, serum creatinine
POMPP (prediction of mortality in perforated peptic ulcer) score [25]	Patients with perforated peptic ulcer	30-day mortality	Albumin, urea
Mannheim Peritonitis Index [16]	General peritonitis	Preoperative prediction of outcome	Organ failure
APACHE II (acute physiology and chronic health evaluation II) [26]	Critically ill patients	Prediction of outcome in ICU patients	White blood cell count, creatinine, potassium, sodium
SAPS II (simplified acute physiology score II) [27]	Critically ill patients	Prediction of outcome in ICU patients	White blood cell count, bilirubin, urea, potassium, sodium
MPM II (mortality probability models) [28]	Critically ill patients	Prediction of outcome for ICU patients	Liver failure, renal insufficiency
POSSUM (physiological and operative severity score for the enumeration of mortality and morbidity) [29]	Surgical patients	Prediction of mortality	White blood cell count, haemoglobin, urea, potassium, sodium
CORES (calculation of post-operative risk in emergency surgery) [30]	Patients who underwent emergency surgery	In-hospital mortality	White blood cell count, urea, platelet count
MODS (multiple organ dysfunction score) [31]	Critically ill patients	Prediction of mortality and outcome for ICU patients	Serum creatinine, platelet count

(AUC) was performed. Mann-Whitney tests were performed to assess differences between subgroups regarding numerical outcomes (hospital and ICU stay) in patients who had not died in hospital, to remove the effect of censoring of stay due to hospital mortality. A p-value of <0.05 was considered statistically significant.

Approval to conduct the research was granted by the Health Sciences Research Ethics Committee (HSREC) of the UFS (ethics clearance number UFS-HSD2019/0018/2506). Permission for the research was also obtained from the Free State Province Department of Health, the NHLS and the chief executive officer (CEO) of Pelonomi Hospital. Due to the retrospective nature of the study and the use of existing database records, obtaining patient informed consent was not required. No identifiable patient information was recorded.

Results

Over the 5-year study period, 194 patients of whom 188 met the inclusion criteria were identified. Three patients were excluded due to missing admission laboratory values, two due to confirmed malignancy and one due to surgery for suspected perforated peptic ulcer without confirmation of perforation. Demographic characteristics showed that our patient cohort had a median age of 46 years, ranging between 15 and 87 years. The biological sex distribution showed a male predominance ($n = 134$; 71.3 %).

The median values and IQRs of laboratory variables on admission, as well as cases with in-hospital mortality and ICU admission, are shown in Table 2.

The median length of hospital stay was 7 days (range 1–94 days) and 59 (31.4 %) patients were admitted to the ICU. Post-operative in-hospital mortality was found to be 25.0 % ($n = 47$). The age distribution of all patients as well for patients who had died and those admitted to ICU are illustrated in Fig. 1. The mortality for patients admitted to the ICU was 64.4 % ($n = 38$). The mortality rate in our group of patients ≤50 years of age was 16.8 %, compared to 37.3 % in patients aged >50 years.

In terms of predicting the two categorical outcomes of in-hospital mortality and ICU admission, abnormal haemoglobin, platelet count, urea, creatinine and potassium levels were all found to be statistically significant in univariate analysis. Abnormal albumin levels showed a statistical significance in predicting ICU admission but not in-hospital mortality. Tables 3 and 4 summarise the different p-values and percentage of patients according to outcome categories of in-hospital mortality and ICU admission.

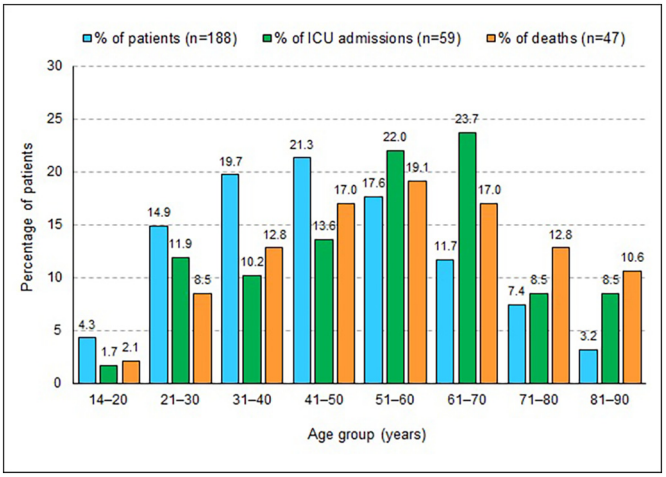

Fig. 1. Age, intensive care unit (ICU) admission and mortality distribution.

Logistic regression analysis was applied to these statistically significant outcomes using age and biological sex as confounders. p-Values, estimated odds ratios (ORs) and 95 % confidence intervals (CI) of logistic regression analysis for in-hospital mortality and ICU admission are shown in Table 5.

For in-hospital mortality, age ($p = 0.0091$), haemoglobin ($p = 0.0432$) and creatinine ($p < 0.0001$) were significant in multivariate analysis with AUC 0.83. For ICU admission, albumin was excluded from the model due to a large number of missing values and no clear independent relation to outcome could be confirmed. Multivariate analysis significant parameters for ICU admission were age ($p = 0.0441$), biological sex ($p = 0.0352$), platelet count ($p = 0.0409$) and creatinine ($p < 0.0001$) with AUC 0.84. The sensitivity, specificity and predictive values of different cut-off values of the laboratory variables were calculated for predicting in-hospital mortality and ICU admission. Values with the highest success in prediction are demonstrated in Table 6.

Secondary outcome analyses for length of hospital and ICU stay (in patients who did not die in hospital) showed urea ($p = 0.0048$), creatinine ($p = 0.0055$) and albumin ($p = 0.0416$) to be statistically significant in predicting length of ICU stay. Although all subgroups for these three variables had a median ICU stay of 0 (zero) days, some differences were observed regarding 75th percentiles and differences were due to

Table 2
Admission laboratory values of patients with perforated peptic ulcer.

Laboratory variable	Median (n[a])	Median: In-hospital mortality (n)	Median: ICU admission (n)
Haemoglobin (g/dL) NRR: 14.3–18.3 g/dL	14.30 (N = 188) IQR: 12.10–16.15	12.60 (N = 47) IQR: 10.90–15.20	12.60 (N = 59) IQR: 10.80–15.60
Haematocrit (L/L) NRR: 0.43–0.55 L/L	0.44 (N = 184) IQR: 0.38–0.50	0.41 (N = 47) IQR: 0.34–0.48	0.41 (N = 59) IQR: 0.34–0.48
WCC ($\times 10^9$/L) NRR: 4.0–10.0 $\times$ 10^9/LR	10.96 (N = 188) IQR: 7.17–15.33	9.72 (N = 47) IQR: 6.43–14.02	9.26 (N = 59) IQR: 5.82–15.25
Platelet count ($\times 10^9$/L) NRR: 171–388 $\times$ 10^9/L	324 (N = 188) IQR: 231.50–408.50	341 (N = 47) IQR: 227.00–452.00	332 (N = 59) IQR: 234.00–457.00
Urea (mmol/L) NRR: 2.1–7.1 mmol/L	8 (N = 187) IQR: 4.90–12.70	13 (N = 47) IQR: 9.10–20.70	12.6 (N = 58) IQR: 8.00–20.00
Creatinine (μmol/L) NRR: 64–104 μmol/L	95 (N = 177) IQR: 71.00–162.00	181 (N = 47) IQR: 118.00–293.00	176.50 (N = 58) IQR: 118.00–293.00
Sodium (mmol/L) NRR: 136–145 mmol/L	137 (N = 188) IQR: 133.00–141.50	137 (N = 47) IQR: 133.00–142.00	137 (N = 59) IQR: 133.00–143.00
Potassium (mmol/L) NRR: 3.5–5.1 mmol/L	4.30 (N = 186) IQR: 3.90–5.00	4.90 (N = 47) IQR: 4.00–5.40	4.90 (N = 59) IQR: 4.00–5.40
C-reactive protein (mg/L) NRR: 0–5 mg/L	170 (N = 150) IQR: 63.00–280.00	246 (N = 35) IQR: 136.00–305.00	246 (N = 45) IQR: 181.00–302.00
Albumin (g/L) NRR: 35–52 g/L	25.0 (N = 119) IQR: 17.00–32.00	20.0 (N = 43) IQR: 14.00–29.00	19.0 (N = 58) IQR: 14.00–26.00

[a] n: number of patients; IQR: interquartile range; NRR: normal reference range used by the NHLS.

Table 3
p-Values calculated for prediction of in-hospital mortality by categorised laboratory values.

Laboratory variable	Outcome	% low (n[a])	% normal (n)	% high (n)	*p*-Value
Haemoglobin (g/dL) NRR: 14.3–18.3 g/dL	Deceased	68.1 % (32)	19.2 % (9)	12.8 % (6)	0.0016
	Survived	43.3 % (61)	48.9 % (69)	7.8 % (11)	
Haematocrit (L/L) NRR: 0.43–0.55 L/L	Deceased	57.5 % (27)	31.9 % (15)	10.6 % (5)	0.0996
	Survived	40.9 % (56)	49.6 % (68)	9.5 % (13)	
WCC ($\times 10^9$/L) NRR: 4.0–10.0 $\times$ 10^9/L	Deceased	14.9 % (7)	38.3 % (18)	46.8 % (22)	0.2169
	Survived	7.1 % (10)	36.2 % (51)	56.7 % (80)	
Platelet count ($\times 10^9$/L) NRR: 171–388 $\times$ 10^9/L	Deceased	14.9 % (7)	48.9 % (23)	36.2 % (17)	0.0067
	Survived	4.3 % (6)	70.9 % (100)	24.8 % (35)	
Urea (mmol/L) NRR: 2.1–7.1 mmol/L	Deceased	2.1 % (1)	12.8 % (6)	85.1 % (40)	<0.0001[b]
	Survived	0 % (0)	54.3 % (76)	45.7 % (64)	
Creatinine (μmol/L) NRR: 64–104 μmol/L	Deceased	4.3 % (2)	12.8 % (6)	83.0 % (39)	<0.0001
	Survived	18.5 % (24)	48.5 % (63)	33.1 % (43)	
Sodium (mmol/L) NRR: 136–145 mmol/L	Deceased	40.4 % (19)	51.1 % (24)	8.5 % (4)	0.8207
	Survived	35.5 % (50)	56.0 % (79)	8.5 % (12)	
Potassium (mmol/L) NRR: 3.5–5.1 mmol/L	Deceased	6.4 % (3)	53.2 % (25)	40.4 % (19)	0.0008
	Survived	10.1 % (14)	75.5 % (105)	14.4 % (20)	
C-reactive protein (mg/L) NRR: 0–5 mg/L	Deceased	–	5.7 % (2)	94.3 % (33)	0.7331[b]
	Survived	–	8.7 % (10)	91.3 % (105)	
Albumin (g/L) NRR: 35–52 g/L	Deceased	90.7 % (39)	9.3 % (4)	–	0.0996
	Survived	79.0 % (60)	21.1 % (16)	–	

NRR: normal reference ranged used by the NHLS.
[a] n: number of patients.
[b] *p*-Value derived from Fisher's exact test; all other *p*-values derived from chi-square.

differences in ICU admission (as shown in Table 4). Potassium ($p = 0.0167$) and albumin ($p = 0.0231$) were statistically significant in predicting length of hospital stay. Patients with low potassium had a median hospital stay of 8 days (IQR 6–11 days), those with high potassium levels a median stay of 8.5 days (IQR 6–11 days) and those with normal potassium levels a median hospital stay of 6 days (IQR 5–9 days). Patients with low albumin levels had a median stay of 8 days (IQR 6–15 days) compared to patients with a normal albumin level who had a median stay of 7 days (IQR 4–8 days).

Discussion

The diagnosis of perforated peptic ulcer disease is based on a combination of history, clinical and radiological findings. Surgical intervention with explorative laparotomy, ulcer biopsy, primary repair and omentoplasty are the preferred surgical modalities in the management of perforated peptic ulcers in our institution.

Our study included all patients presenting in the defined population with no selection in referral; therefore, we expected our mortality rate (25.0 %) to be similar to the mortality rate of 1.3–40 % among patients with a perforated peptic ulcer reported in the literature [2,3,7,9–21].

Investigations into risk factors for perforation are complicated by the wide variation in demographics, socioeconomic status, *Helicobacter pylori* prevalence and medication and substance use in different population groups [18]. Cohorts from other African countries show a male predominance of 6–13:1 to females [18]. In developing countries, young (predominantly male) smokers represent the biggest patient group, whereas in developed countries, elderly patients (showing an increase in females) with other co-morbidities and associated use of NSAIDs are more common [8,13,22]. Significant inequality in South Africa contributed to a wide spectrum of socio-economic circumstances in our study population and variable population groups might have been included [32]. Our age distribution, with a median of 46 years (range 15–87 years), was similar to other South African study demographics as compared to an older age distribution reported in the literature

Table 4
p-Values calculated for prediction of intensive care unit (ICU) admission by categorised laboratory values.

Laboratory variable	Outcome	% low (n[a])	% normal (n)	% high (n)	*p*-Value
Haemoglobin (g/dL) NRR: 14.3–18.3 g/dL	ICU	64.4 % (38)	27.1 %(16)	8.5 % (5)	0.0167
	Ward	42.6 % (55)	48.1 % (62)	9.3 % (12)	
Haematocrit (L/L) NRR: 0.43–0.55 L/L	ICU	55.9 % (33)	33.9 % (20)	10.2 % (6)	0.0959
	Ward	40.0 %(50)	50.4 % (63)	9.6 % (12)	
WCC ($\times 10^9$/L) NRR: 4.0–10.0 $\times$ 10^9/L	ICU	15.3 % (9)	40.7 % (24)	44.1 % (26)	0.0583
	Ward	6.2 % (8)	34.9 % (45)	58.9 % (76)	
Platelet count ($\times 10^9$/L) NRR: 171–388 $\times$ 10^9/L	ICU	11.9 % (7)	49.2 % (29)	39.0 % (23)	0.0052
	Ward	4.7 % (6)	72.9 % (94)	22.5 % (29)	
Urea (mmol/L) NRR: 2.1–7.1 mmol/L	ICU	0 % (0)	17.2 % (10)	82.8 % (48)	<0.0001[b]
	Ward	0.8 % (1)	55.8 % (72)	43.4 % (56)	
Creatinine (μmol/L) NRR: 64–104 μmol/L	ICU	3.5 % (2)	17.2 (10)	79.3 % (46)	<0.0001
	Ward	20.2 % (24)	49.6 % (59)	30.3 % (36)	
Sodium (mmol/L) NRR: 136–145 mmol/L	ICU	35.6 % (21)	54.2 % (32)	10.2 % (6)	0.8557
	Ward	37.2 % (48)	55.0 % (71)	7.8 % (10)	
Potassium (mmol/L) NRR: 3.5–5.1 mmol/L	ICU	6.8 % (4)	54.2 % (32)	39.0 % (23)	0.0002
	Ward	10.2 %(13)	77.2 % (98)	12.6 % (16)	
C-reactive protein (mg/L) NRR: 0–5 mg/L	ICU	–	6.7 % (3)	93.3 % (42)	1.0000[b]
	Ward	–	8.6 % (9)	91.4 % (96)	
Albumin (g/L) NRR: 35–52 g/L	ICU	93.1 % (54)	6.9 % (4)	–	0.0048
	Ward	73.8 % (45)	26.2 % (16)	–	

[a] n: number of patients.
[b] *p*-Value derived from Fisher's exact test; all other *p*-values derived from chi-square.

Table 5
Logistic regression analysis using age and gender as confounders for in-hospital mortality and ICU admission.

Variable	Odds ratio (OR)	95 % CI for OR	*p*-Value
In-hospital mortality			
Age	1.03	1.01–1.06	0.0091
Abnormally low haemoglobin	2.88	1.15–7.20	0.0432
Abnormally high haemoglobin	4.36	0.98–19.39	
Abnormally high creatinine	7.76	2.90–20.74	<0.0001
ICU admission			
Age	1.03	1.00–1.05	0.0441
Sex: male versus female	0.37	0.15–0.93	0.0352
Abnormally low platelet count	2.21	0.58–8.43	0.0409
Abnormally high platelet count	2.94	1.24–7.01	
Abnormally high creatinine	6.90	2.87–16.61	<0.0001

[21]. We had a male predominance (2.48:1) but it was not as high as similar patient groups in South African and other African series, and closer to distribution ratios reported before [18,21]. Our median length of hospital stay of 7 days (range 1–94 days) was similar to findings in other studies [33,34].

There is still no recognised agreement on a standard scoring system. Establishing an optimal prediction model in terms of outcome for patients with perforated peptic ulcers has been investigated [6,18]. The reason for none of the multiple scoring systems being widely accepted in clinical practice could be due to the complexity, non-specificity or subjective points of these scoring systems [25]. The goals of being easy to calculate, accurate in predicting outcome and being reproducible across different populations have not been comprehensively satisfied by any of the currently available scores [23]. Patel et al. [35] reported that although the Boey score was found to be more practical to apply, the PULP score proved to be a more accurate indicator of mortality. They did confirm, however, that increased serum creatinine, in addition to preoperative shock, pre-existing comorbidities and delayed surgery of >24 h, was a significant indicator of a poor outcome in patients with perforated peptic ulcer [35].

Due to the wide non-urban referral area of our hospital, a large number of our patients is admitted with a late presentation that already falls outside the 24-hour window period from first symptoms to surgery. Literature from South Africa reports a late presentation in patients with perforated peptic ulcers outside of the 24-hour window from the onset of symptoms to being admitted to hospital [21]. Record bias in terms of pre-hospital data has been reported in retrospective studies. Patient recall bias in terms of medical and complaint history could also be possible and patients with pre-existing peptic ulcer disease might experience pain or symptoms for some time and are therefore unable to pinpoint exactly when pain was exacerbated [36]. Accurate patient history might not be possible due to the clinical condition of the patient (e.g., decrease in level of consciousness, elderly patients). This will influence obtaining the patient's medical history in terms of other comorbidities and medication use at the time of admission [25].

Table 6
Success in predicting in-hospital mortality of a value greater or equal to mentioned value for urea and creatinine, and ICU admission of a value greater or equal to mentioned value for urea and creatinine and a value smaller or equal for albumin.

Variable	Value	PPV	NPV	Sensitivity	Specificity	AUC
In-hospital mortality						
Urea	10.9 mmol/L	56.9 %	89.2 %	70.2 %	82.1 %	0.79
Creatinine	109 μmol/L	47.5 %	90.7 %	80.9 %	67.7 %	0.80
ICU admission						
Urea	8.9 mmol/L	55.3 %	85.6 %	72.4 %	73.6 %	0.74
Creatinine	136 μmol/L	66.2 %	86.7 %	74.1 %	81.5 %	0.82
Albumin	30 g/L	61.7 %	78.9 %	86.2 %	49.2 %	0.78

PPV: positive predictive value; NPV: negative predictive value; AUC: area under the receiver operating characteristic (ROC) curve.

All these risk factors have been questioned due to insufficient objectivity and have been reported to lack sensitivity and specificity [35]. However, these risk factors still form part of some scoring systems (e.g., PULP score, Mannheim Peritonitis score, Hacettepe score) previously described in the prediction of patient outcome [15,16].

The POMPP score [25] was developed in 2015 as a practical scoring system to assist in calculating mortality risk in patients with perforated peptic ulcers. It indicated age, albumin and urea levels to be three variables that are statistically relevant in multivariate analysis. This new scoring system compared well to the ASA, PULP and Boey scoring systems, but was found less complex as it incorporated only age and two admission laboratory values (albumin and urea) [25]. We found urea ($p < 0.0001$) to be a significant predictor of both mortality and ICU admission, and albumin ($p = 0.0048$) to predict ICU admission in univariate analysis. Due to a large number of missing albumin values ($n = 69$) in our study, it could unfortunately not be included in the multivariate analysis.

A model to calculate post-operative risk specifically for emergency surgery (CORES) was developed in Japan in 2012 [30]. It uses five preoperative variables that include white blood cell count (WCC), platelet count and blood urea nitrogen as laboratory values. The model is able to reproducibly predict post-operative mortality in the validation and multicentre subgroups. It was postulated that the better prediction in the general surgery patient subset compared to the P-POSSUM score could be due to the inclusion of platelet count. Thrombocytopenia has been shown to be a risk factor for mortality in ICU patients and is the most commonly cited manifestation of haematological dysfunction [30,31]. Patients with a high platelet count (>300,000 cells/μL) also had notably higher mortality rates demonstrated in the study used to develop the CORES model [30]. We found both thrombocytopenia (OR 2.21 [95 % CI 0.58–8.43]) and thrombocytosis (OR 2.94 [95 % CI 1.24–7.01]) to be significant variables after multivariate analysis in predicting ICU admission.

A study involving an African population in Côte d'Ivoire [17] who had operative interventions for perforated peptic ulcer disease, showed a high median WCC ($p < 0.0001$), low levels of sodium (134 versus 137 mmol/L, $p = 0.02$) and low potassium levels (3.6 versus 3.7 mmol/L, $p = 0.01$) in patients that had postoperative complications or mortality compared to those without major complications or mortality [17]. We did not find WCC or sodium to be significant variables in our patient group, but did find abnormal potassium ($p = 0.0008$) to be significant in predicting mortality in univariate analysis.

The development of CORES, Hacettepe, PULP and Jabalpur scores all demonstrated elevated creatinine as a significant risk factor [15,16,24,30]. We found abnormally high creatinine to be the strongest single predictor of outcome in patients with perforated peptic ulcers. It demonstrated an OR of 7.76 [95 % CI 2.90–20.74; $p < 0.0001$] in predicting in-hospital mortality and an OR of 6.90 [95 % CI 2.87–16.61; $p < 0.0001$] in predicting ICU admission. This is substantially higher than the ORs demonstrated in developing the PULP score (OR 2.25 [95 % CI 1.78–2.84]) [15]. Elevated creatinine can only be a surrogate marker for septic shock and multi-organ dysfunction syndrome, including acute kidney injury, and further investigation into causality of this finding might be needed at a later stage.

Our study demonstrated that a urea level of ≥10.9 mmol/L had a sensitivity of 70.2 % and specificity of 82.1 % (area under curve [AUC] 0.79), while a creatinine level of ≥109 μmol/L had a sensitivity of 80.9 % and specificity of 67.7 % (AUC 0.80) in predicting in-hospital mortality.

The PULP score demonstrated an OR of 1.13 [95 % CI 0.80–1.61] for a haemoglobin level of <6 mmol/L in predicting mortality [15]. We found that both abnormally low (OR 2.88 [95 % CI 1.15–7.20]) and high (OR 4.36 [95 % CI 0.98–19.39]) haemoglobin levels were significant in predicting in-hospital mortality.

Our study also validated age as a significant predictor of the patient's prognosis. It showed an OR of 1.03[95 % CI 1.00–1.06]; $p = 0.0091$ for predicting in-hospital mortality and an OR of 1.03 [95 % CI 1.00–1.05];

$p = 0.0441$ for predicting ICU admission. The importance of advanced age as an independent risk factor has been emphasised in the literature [3,7,9,25,33].

A notable part of the findings observed in our specific patient cohort was supported by previously identified outcome predictors reported in the literature. Discrepancies could most likely be attributed to differences in demographic factors and mortality in other settings. These results will assist in the practical application of readily available laboratory values in predicting outcomes in patients with perforated peptic ulcers. It can lead to improved clinical decisions and cost-benefit strategies. Furthermore, it will promote optimal management and facilitate better assignment of resources such as theatre space and consultant coverage.

Limited ICU bed availability in most healthcare settings emphasises the importance of individual risk stratification. We had an alarmingly high mortality rate in our ICU admission group and prioritising a different patient group with better prognosis for ICU admission could have shown better outcomes. Scoring systems should be easy to calculate and have a high degree of accuracy in predicting adverse outcomes, which have been proven difficult to materialise in this patient group. Patients identified as being at higher risk could have earlier access to organ support, intensive care and more aggressive resuscitation. Outcomes can then be improved based on individual risk stratification. It has been proven that additional perioperative care and management protocols for high-risk patients reduce in-hospital mortality [10,25]. Knowledge of significant independent risk factors by the surgeon will assist in confident judgement about operative planning and appropriateness [16]. This awareness will also improve patient counselling in terms of risks, possible complications and outcome expectations. Obviously, an individual predictor cannot be ascribed to a single patient, but the presence of a significant or more than one risk factor presents a much higher mortality risk compared to patients with no risk factors [6].

These findings can also be used in combination with other preoperative information or in further prospective studies to develop appropriate prediction and scoring systems for this healthcare setting, or applied in different populations as a comparison. Most of the studies available in the literature had been conducted mainly in western and Asian countries [17]. In the era of hand-held electronic devices and smartphones, more complex scoring systems might be easier to calculate at the bedside than before [23]. It might be difficult to develop a universally reproducible scoring system due to geographical variation in age, biological sex and patterns of presentation [18]. Laboratory values, however, have the advantage of being an objective variable not influenced by subjective interpretation and are therefore ideal for validation between different patient cohorts and demographic regions [6].

Although the study involved a consecutive cohort, a limitation could be that it was a retrospective, single-centre study. An additional limitation was that both gastric and duodenal ulcers have been grouped under the umbrella of peptic ulcer disease, because information regarding the anatomical location of these ulcers during surgery was not available, even though aetiological factors and pathophysiological processes may differ. Another shortcoming was that history of NSAIDs and steroids use as well as prior *H. pylori* infection were not included in the data collected, and although not part of the primary aim of the study, might still have been useful in determining a more accurate patient profile. An advantage is that we had minimal missing data due to consistent laboratory records. This might be more of a problem in future studies using other perioperative variables depending on pre-hospital and hospital records. Laboratory values might merely be indicators for other underlying factors such as a chronic disease. Further investigation into causality from the findings in the study might therefore be warranted at a later stage. The long-term outcome after hospital discharge of our patient group was also not assessed. Logistic regression was used to minimise confounding variables. Some of the calculated 95 % CIs were wide and indicative of low statistical precision. Other reference ranges for abnormal values and definitions or categorisation of demographic variables might have produced different results.

Conclusion

All laboratory values might not be exact in predicting mortality, although we found that routine admission laboratory values do most certainly contribute to building a risk stratification model for this specific patient group in our healthcare setting. A locally applicable risk prediction model with the inclusion of other risk factors should be developed and validated in future prospective studies. This study simply questioned whether admission laboratory values in isolation could be regarded as trustworthy to assist with predicting the outcome in a patient with a perforated peptic ulcer. Admission laboratory values are valuable in predicting surgical outcomes and play a crucial role in our approach and management of the patient from the time of admission.

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CRediT authorship contribution statement

Conceptualisation: WM, EA-C; methodology: WM, EA-C; data collection, curation, project administration; WM; formal analysis: GJ; writing – original draft: WM; writing – review & editing: WM, EA-C; GJ; supervision: EA-C.

Conflict of interest

The authors declare that they have no potential competing interests to disclose.

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Ethics statement

Approval to conduct the research was granted by the Health Sciences Research Ethics Committee (HSREC) of the UFS (ethics clearance number UFS-HSD2019/0018/2506). Permission for the research was also obtained from the Free State Province Department of Health, the NHLS and the chief executive officer (CEO) of Pelonomi Hospital. Due to the retrospective nature of the study and the use of existing database records, obtaining patient informed consent was not required. No identifiable patient information was recorded.

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