Are Admission Laboratory Values in Isolation Valuable in Predicting Surgical Outcome in Patients With Perforated Peptic Ulcers: A Retrospective, Cohort Analytical, Observational Study

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ARE ADMISSION LABORATORY VALUES IN ISOLATION VALUABLE IN PREDICTING SURGICAL OUTCOME IN PATIENTS WITH PERFORATED PEPTIC ULCERS: A RETROSPECTIVE, COHORT ANALYTICAL, OBSERVATIONAL STUDY

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Abstract

Background:

Perforated peptic ulcer carries noteworthy mortality, and admission status is a significant prognosticator thereof. Laboratory values are objective and readily available and, therefore, ideal for risk stratification. The objective of the study is to calculate the predictive value of admission laboratory values in patients with perforated peptic ulcers.

Methods:

A retrospective, cohort analytical, observational study was performed. All patients with surgically confirmed perforated peptic ulcers at Pelonomi Tertiary Hospital from July 2014 to June 2019 were considered. Demographic data and admission laboratory values were collected from hospital and laboratory electronic databases and theatre books. Outcomes measured were in-hospital mortality, ICU admission and length of stay in ICU and hospital. The significance of categorical variables was calculated by Chi-square and Fisher's exact test. Logistic regression analysis considered univariately statistically significant variables. A p-value of < 0.05 was considered statistically significant.

Results:

Over the 5-year period, 188 patients met the inclusion criteria. The median age was 46 years (15-87), with a male predominance of 71.3 % (N=134). The median length of hospital stay was seven days (1-94), and 31.4% (N=59) of patients were admitted to the Intensive Care Unit. Operative in-hospital mortality was 25.0% (N=47).

Predicting the two categorical outcomes of in-hospital mortality and ICU admission, abnormal haemoglobin, platelet count, urea, creatinine, and potassium were statistically significant in univariate analysis. For in-hospital mortality, age (OR 1.03), haemoglobin (OR

4.36) and creatinine (OR 7.76) were significant in multivariate analysis, and for ICU admission age (OR 1.03), platelet count (OR2.94) and creatinine (OR 6.90). Urea ≥ 10.9mmol/L showed a sensitivity of 70.2% and specificity of 82.1% (AUC 0.79), and creatinine ≥ 109umol/L a sensitivity of 80.9% and specificity of 67.7% (AUC 0.80) in predicting in-hospital mortality.

Conclusions:

The mortality rate in patients with perforated peptic ulcer disease is still substantial. Admission laboratory values show statistical significance as outcome indicators and are valuable to assist in predicting prognostication. Abnormal high serum creatinine was the strongest single predictor of both mortality and ICU admission.

Keywords

Peptic ulcer perforation, outcome prediction, mortality, laboratory values, emergency surgery

Background

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

The incidence of perforation is 4-10/100 000 population per annum and can be the first hospital presentation of 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 more than 70% of deaths associated with peptic ulcer disease.[8] Sepsis and septic shock are common, and a frequent ultimate cause of mortality.[9–11] Perforated peptic ulcer carries a mortality of 1.3% to 40%. [2,3,16–21,7,9–15]

Admission status has been described as a significant prognostic indicator in patients with peptic ulcer perforation.[13] It is imperative that diagnosis is made early, resuscitation efforts initiated swiftly and rapid surgical intervention initiated 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 described as part of the sepsis syndrome.[3] The diagnosis of a perforated peptic ulcer cannot be made using laboratory values in isolation, and these values are non-specific.[12] Laboratory values are however, good indicators of organ dysfunction, local and systemic inflammation. They are also used to rule out other pathologies on the differential diagnosis, like acute pancreatitis.[8,18,22] The biggest advantage for the use of laboratory values in risk stratification is that they are objective in nature, routinely done, and readily available.[6] Laboratory values form part of most perforated ulcer and other prognostic scoring systems used currently: (Table 1)[3,23]:

Table 1: Laboratory values that form part of scoring systems used for prediction models in patients with perforated peptic ulcers:

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	30-day mortality	Serum creatinine

	ulcer		
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	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 score)[29]	Surgical patients	Prediction of mortality	White blood cell count, Haemoglobin, Urea, Potassium, Sodium
CORES (Calculation of postoperative risk in emergency surgery) [30]	Patients who underwent emergency surgery	In-hospital mortality	White blood cell count, urea, platelet count
Multiple organ dysfunction score (MODS) [31]	Critically ill patients	Prediction of mortality and outcome for ICU patients	Serum creatinine, platelet count

Scoring systems are used to provide an objective description of the patient's condition at a specific stage in the disease process to try and assist the physician with the diagnosis, give guidance in the course that the disease is taking in the specific patient and help the surgeon to follow 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 are of any value in isolation and can they 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 ICU admission, length of stay in ICU and length of stay in hospital) 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- 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 provides the bulk of the acute care surgical and trauma services for the Free State Province in South Africa.

Exclusion criteria were:

- Histological confirmed malignant perforations
- Traumatic or iatrogenic perforations
- Perforations due to caustic ingestion or foreign bodies
- Perforations found during an autopsy
- Patients managed conservatively without surgical intervention

- Patients who had surgery but no confirmation of perforated ulcer
- Patients younger than 13 years

In-hospital mortality was defined as any death occurring during or after surgical intervention before hospital discharge.

Data were collected for all patients who met the inclusion criteria. Demographic data was 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 Department of Surgery Statistical Database and Pelonomi Hospital theatre record books were used to verify the concordance of collected data.

Demographic data included age and sex.

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

- Full blood count (Haemoglobin, Haematocrit, White cell count, Platelets)
- Renal function (Urea and Creatinine)
- Electrolytes (Sodium and Potassium)
- Inflammatory markers (C-reactive Protein- CRP)
- Albumin

The reference range for normal laboratory values used by the South African NHLS (see additional file 1) was applied to the laboratory values with values outside the normal range categorized as abnormal low or abnormal high.

Data captured was recorded on the researcher's approved data sheet and onto an Excel sheet that serves as a second copy of all data.

The analysis was done by the Department of Biostatistics University of Free State. Numerical variables were summarized by medians and interquartile ranges (IQR) due to skew distributions and categorical variables by frequencies and percentages. 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% CI. A p-value of < 0.05 was considered statistically significant. Calculation of sensitivity, specificity, positive and negative predictive values were done.

Results:

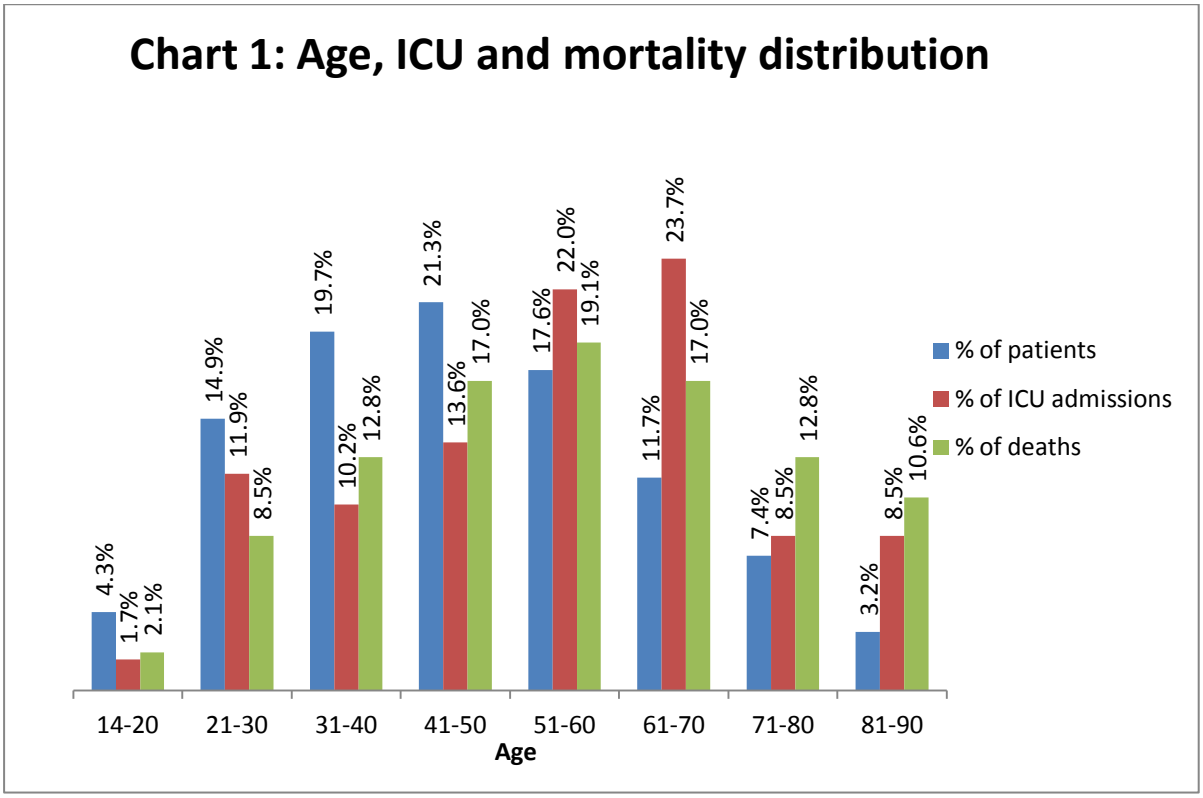
Over the 5-year study period, we identified 194 patients, of whom 188 met the inclusion criteria. Three patients were excluded due to missing admission laboratory values, two due to confirmed malignancy and one due to surgery for suspicion of PPU without confirmation of perforation. Demographic characteristics showed our patient cohort had a median age of 46 years with a range between 15 and 87 years. The gender distribution showed a male predominance of 134 (71.3%) versus 54 (28.7%) female patients.

The median values and interquartile ranges (IQR) of laboratory variables on admission as well as cases with in-hospital mortality and ICU admission are shown in Table 2.

Table 2: Admission laboratory values

Laboratory variable	Median (N)	Median: In-hospital mortality (N)	Median: ICU admission (N)
Hemoglobin (g/dL)	14.30 (N=188)	12.60 (N=47)	12.60 (N=59)
	IQR: 12.10-16.15	IQR: 10.90-15.20	IQR: 10.80-15.60
Haematocrit (L/L)	0.44 (N=184)	0.41 (N=47)	0.41 (N=59)
	IQR: 0.38-0.50	IQR: 0.34-0.48	IQR: 0.34-0.48
WCC ($x10^9$/L)	10.96 (N=188)	9.72 (N=47)	9.26 (N=59)
	IQR: 7.17-15.33	IQR: 6.43-14.02	IQR: 5.82-15.25
Platelet count ($x10^9$/L)	324 (N=188)	341 (N=47)	332 (N=59)
	IQR: 231.50-408.50	IQR: 227.00-452.00	IQR: 234.00-457.00
Urea (mmol/L)	8 (N=187)	13 (N=47)	12.6 (N=58)
	IQR: 4.90-12.70	IQR: 9.10-20.70	IQR: 8.00-20.00
Creatinine (umol/L)	95 (N=177)	181 (N=47)	176.50 (N=58)
	IQR: 71.00-162.00	IQR: 118.00-293.00	IQR: 118.00-293.00
Sodium (mmol/L)	137 (N=188)	137 (N=47)	137 (N=59)
	IQR: 133.00-141.50	IQR: 133.00-142.00	IQR: 133.00-143.00
Potassium (mmol/L)	4.30 (N=186)	4.90 (N=47)	4.90 (N=59)
	IQR: 3.90-5.00	IQR: 4.00-5.40	IQR: 4.00-5.40
C-reactive protein	170 (N=150)	246 (N=35)	246 (N=45)
(mg/L)	IQR: 63.00-280.00	IQR: 136.00-305.00	IQR: 181.00-302.00
Albumin (g/L)	25.0 (N=119)	20.0 (N=43)	19.0 (N=58)
	IQR: 17.00-32.00	IQR: 14.00-29.00	IQR: 14.00-26.00

The median length of hospital stay was seven days (range 1-94), and 59 (31.4%) patients were admitted to the Intensive Care Unit. Operative in-hospital mortality was found to be 25.0% (N=47). Age, mortality and ICU admission distribution are illustrated in Chart 1. The mortality for patients admitted to the Intensive Care Unit was 64.4% (N=38).



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

Table 3: p-values calculated for the prediction of in-hospital mortality by categorized laboratory values

Laboratory variable		*% Low (N)*	*% Normal (N)*	*% High (N)*	*p-value*
Haemoglobin	Mortality	68.1% (32)	19.2 % (9)	12.8% (6)	0.0016
	Survived	43.3% (61)	48.9% (69)	7.8% (11)	
Haematocrit	Mortality	57.5% (27)	31.9% (15)	10.6% (5)	0.0996
	Survived	40.9% (56)	49.6% (68)	9.5% (13)	
WCC	Mortality	14.9% (7)	38.3% (18)	46.8% (22)	0.2169
	Survived	7.1% (10)	36.2% (51)	56.7% (80)	
Platelets	Mortality	14.9% (7)	48.9% (23)	36.2% (17)	0.0067
	Survived	4.3% (6)	70.9% 100)	24.8% (35)	
Urea	Mortality	2.1% (1)	12.8% (6)	85.1% (40)	<.0001*
	Survived	0% (0)	54.3% (76)	45.7% (64)	
Creatinine	Mortality	4.3% (2)	12.8% (6)	83.0% (39)	<.0001
	Survived	18.5% (24)	48.5% (63)	33.1% (43)	
Sodium	Mortality	40.4% (19)	51.1% (24)	8.5% (4)	0.8207
	Survived	35.5% (50)	56.0% (79)	8.5% (12)	
Potassium	Mortality	6.4% (3)	53.2% (25)	40.4% (19)	0.0008
	Survived	10.1% (14)	75.5% (105)	14.4% (20)	
C reactive peptide	Mortality	-	5.7 % (2)	94.3% (33)	0.7331*
	Survived	-	8.7% (10)	91.3% (105)	
Albumin	Mortality	90.7% (39)	9.3% (4)	-	0.0996
	Survived	79.0% (60)	21.1% (16)	-	

* P-value derived from Fisher's Exact Test all others derived from Chi-square

Table 4: p-values calculated for the prediction of ICU admission by categorized laboratory values

Laboratory variable		*% Low (N)*	*% Normal (N)*	*% High (N)*	*p-value*
Haemoglobin	ICU	64.4% (38)	27.1 %(16)	8.5% (5)	0.0167
	No ICU	42.6% (55)	48.1% (62)	9.3% (12)	
Haematocrit	ICU	55.9% (33)	33.9% (20)	10.2% (6)	0.0959
	No ICU	40.00%(50)	50.4% (63)	9.6% (12)	
WCC	ICU	15.3% (9)	40.7% (24)	44.1% (26)	0.0583
	No ICU	6.2% (8)	34.9% (45)	58.9% (76)	
Platelets	ICU	11.9% (7)	49.2% (29)	39.0% (23)	0.0052
	No ICU	4.7% (6)	72.9% (94)	22.5% (29)	
Urea	ICU	0% (0)	17.2% (10)	82.8% (48)	<.0001 *
	No ICU	0.8% (1)	55.8% (72)	43.4% (56)	
Creatinine	ICU	3.5% (2)	17.2 (10)	79.3% (46)	<.0001
	No ICU	20.2% (24)	49.6% (59)	30.3% (36)	
Sodium	ICU	35.6% (21)	54.2% (32)	10.2% (6)	0.8557
	No ICU	37.2% (48)	55.0% (71)	7.8% (10)	
Potassium	ICU	6.8% (4)	54.2% (32)	39.0% (23)	0.0002
	No ICU	10.2%(13)	77.2% (98)	12.6% (16)	
C reactive peptide	ICU	-	6.7 % (3)	93.3% (42)	1.0000 *
	No ICU	-	8.6% (9)	91.4% (96)	
Albumin	ICU	93.1% (54)	6.9% (4)	-	0.0048
	No ICU	73.8% (45)	26.2% (16)	-	

* P-value derived from Fisher's Exact Test all others derived from Chi-square

Logistic regression analysis was applied to the above mentioned statistically significant outcomes using age and gender as confounders. P-values, estimated Odds Ratios and 95%

Confidence Intervals of logistic regression analysis for in-hospital mortality and ICU admission are shown in Tables 5 and 6.

For in-hospital mortality age (p = 0.0091) haemoglobin (p = 0.0432) and creatinine (p < .0001) were significant in multivariate analysis. For ICU admission, albumin was excluded from the model due to many missing values and no clear independent relation to outcome. Multivariate analysis significant parameters for ICU admission were age, gender, platelet count and creatinine.

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

Variable	Odds Ratio	95% CI for OR	*p*-value
Age	1.03	1.01-1.06	0.0091
Abnormal low Hemoglobin	2.88	1.15-7.20	0.0432
Abnormal high Hemoglobin	4.36	0.98-19.39	
Abnormal high Creatinine	7.76	2.90- 20.74	<.0001

Table 6: Logistic regression analysis using age and gender as confounders for ICU admission

Variable	Odds Ratio	95% CI for OR	*p*-value
Age	1.03	1.00-1.05	0.0441
Gender male vs. female	0.37	0.15-0.93	0.0352
Abnormal low Platelet count	2.21	0.58-8.43	0.0409
Abnormal high Platelet count	2.94	1.24-7.01	
Abnormal high Creatinine	6.90	2.87-16.61	<.0001

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 Tables 7 and 8

Table 7: Success in predicting in-hospital mortality of a value greater or equal to the mentioned value for Urea and Creatinine

Variable	Value	PPV	NPV	Sensitivity	Specificity	AUC
Urea	10.9mmol/L	56.9%	89.2%	70.2%	82.1%	0.79
Creatinine	109umol/L	47.5%	90.7%	80.9%	67.7%	0.80

PPV: Positive predictive value; NPV: Negative predictive value; AUC: Area under the ROC curve

Table 8: Success in predicting ICU admission of a value greater or equal to the mentioned value for Urea and Creatinine and a value smaller or equal for Albumin

Variable	Value	PPV	NPV	Sensitivity	Specificity	AUC
Urea	8.9mmol/L	55.3%	85.6%	72.4%	73.6%	0.74
Creatinine	136umol/L	66.2%	86.7%	74.1%	81.5%	0.82
Albumin	30g/L	61.7%	78.9%	86.2%	49.2%	0.78

PPV: positive predictive value; NPV: Negative predictive value; AUC: Area under the ROC curve

Secondary outcome analyses for length of hospital and ICU stay 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 days, some differences were observed regarding 75^{th} percentiles, and differences were

due to differences in ICU admission (as shown in Table 4). Potassium (p = 0.0167) and albumin (p = 0.213) were statistically significant in predicting length of hospital stay. Patients with low potassium had a median hospital stay of 8 days (IQR 6 to 11 days), those with high potassium levels median stay of 8.5 days (IQR 6 to 11 days) and those with normal potassium levels median hospital stay of 6 days (IQR 5 to 9 days). Patients with low albumin levels had a median stay of 8 days (IQR 6 to 15 days) compared to patients with a normal albumin level who had a median stay of 7 days (IQR 4 to 8 days). These were calculated for patients who did not die in hospital.

Discussion:

The diagnosis of perforated peptic ulcer disease is made using a combination of history, clinical and radiological findings. Surgical intervention with explorative laparotomy, ulcer biopsy, primary repair and omentoplasty is the preferred surgical management of perforated peptic ulcers in our institution. This is followed by post-operative Proton Pump Inhibitor and Helicobacter Pylori eradication therapy.

Our study included all presenting patients in the defined population with no referral selection; therefore, we expected our mortality rate (25%) to be similar to mortality reported in literature (1.3-40%). [2,3,16–21,7,9–15]

Investigations into risk factors for perforation are complicated by the wide variation in demographics, socioeconomic status, the prevalence of Helicobacter pylori, and medication and substance use in different population groups.[18] Cohorts from other African countries shows a male predominance of 6-13:1 to females.[18] In developing countries, young (predominantly male) smokers make up the most extensive patient group. In contrast, in the developed world, elderly patients (increase in females) with other comorbidities and the associated use of NSAIDs are more commonly found.[8,13,22] Significant inequality in South

Africa leads to a broad spectrum of socioeconomic circumstances in our study population, and both these population groups might have been included.[32] Our age distribution, the median of 46 years (range 15-87), was similar to other South African study demographics, compared to an older age distribution found in most literature.[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 in the rest of literature.[18,21] Our median length of hospital stay of 7 days (range 1-94) was similar to other studies [33,34].

Perforated peptic ulcers are a multifactor disease, and multiple scoring systems have been suggested and used as outcome predictors.[3] Scoring systems range from simple to complex (combining demographical data, history, vital signs and clinical findings, chosen surgical intervention and management options as criteria), sometimes making practical implementation thereof more difficult.[2,35] The ASA (American Society of Anaesthesiologist physical status classification system) and Boey score are the most commonly used validated scores for patients with perforated peptic ulcers.[22] ICU and other standard surgical scores have also been evaluated in patients with perforated peptic ulcers.[18] Replication of original high positive predictive values of used scores has not always been shown in other study populations, and there is a lack of external cohort validation.[2,18,35] There is still no agreed standard scoring system, and investigation towards an optimal prediction model in terms of outcome for patients with perforated peptic ulcers in today's setting is still not saturated.[6,18] The reason for none of the multiple scoring systems being widely accepted in clinical practice can 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 diverse populations have not been comprehensively satisfied by any score.[23]

Due to the wide rural drainage area of our hospital, a large number of our patients have a late presentation that already falls outside the 24 hour window period at the time of theatre.

Literature from South Africa demonstrates a late presentation in patients with perforated peptic ulcers outside of the 24h window from onset of symptoms.[21] Record bias in terms of pre-hospital data plays a part in retrospective studies. Patient recall bias in terms of medical and complaint history can also be possible. Patients with pre-existing peptic ulcer disease might experience pain or symptoms for some time and are unable to pinpoint exactly when pain is exacerbated.[36] Accurate patient history might not be possible due to the patient's clinical condition (e.g. decrease in level of consciousness, elderly patients), influencing patient medical history in terms of other comorbidities and medication-use at the time of admission.[25] All these risk factors have been questioned due to the lack of objectivity and have been reported to lack sensitivity and specificity.[36] However, these risk factors still form part of scoring systems (PULP score, Mannheim Peritonitis score, Hacettepe score) previously described in the prediction of patient outcome.[15,16]

The POMPP score 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 ASA, PULP and Boey scoring systems but was found less complex as it only made use of age and two admission laboratory values (albumin and urea).[25] We found urea ($p < .0001$) to be significant in predicting mortality and ICU admission and albumin ($p = 0.0048$) to predict ICU admission in univariate analysis.

A model to calculate postoperative risk specifically for emergency surgery (CORES) was developed in Japan in 2012. It uses five preoperative variables: white blood cell count (WCC), platelet count and blood urea nitrogen as laboratory values, and reproducibly predicting postoperative 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, as thrombocytopenia has been

shown as 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) interestingly also had higher mortality rates demonstrated in the study used to develop the CORES model.[30] We found thrombocytopenia (OR 2.212 [95% CI 0.581-8.427]) and thrombocytosis (OR 2.942 [95% CI 1.235-7.009]) both to be significant variables after multivariate analysis in predicting ICU admission.

A contemporary study done among an African population in Côte d'Ivoire who had operative interventions for perforated peptic ulcer disease showed a high median value WCC ($p <$ 0.0001), low level of natraemia (134 vs 137, $p = 0.02$) and low potassium (3.6 vs 3.7, $p =$ 0.01) in patients that had postoperative complications or mortality compared to those without. 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.

Development of CORES, Hacettepe, PULP and Jabalpur scores all demonstrated elevated creatinine as a significant risk factor.[15,16,24,30] We found abnormal high creatinine to be the strongest single predictor of outcome in patients with perforated peptic ulcers. It demonstrated an OR of 7.755 [95% CI 2.899-20.740; p <.0001] in predicting in-hospital mortality and an OR of 6.900 [95% CI 2.866-16.609; p <.0001] in predicting ICU admission. These ratios are much higher than the Odds ratios demonstrated in developing the PULP score (OR 2.25 [95% CI 1.78-2.84]).[15]

Our study demonstrated urea ≥ 10.9mmol/L had a sensitivity of 70.21% and specificity of 82.14% (AUC 0.79), and creatinine ≥ 109umol/L a sensitivity of 80.85% and specificity of 67.69% (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 < 6 mmol/L in predicting mortality.[15] Our study demonstrated abnormal low (OR 2.877 [95% CI 1.149-7.201]) and high (OR 4.363 [95% CI 0.982-19.386]) haemoglobin levels both to be significant in predicting in-hospital mortality.

Our study also validated age as a significant prognosticator. It showed an OR of 1.034[95% CI 1.008-1.061]; p = 0.0091 for predicting in-hospital mortality and an OR of 1.025 [95% CI 1.001-1.051]; p = 0.0441 for predicting ICU admission. The importance of advanced age as an independent risk factor remains as valid as in literature. [3,7,9,25,33]

A large part of our study validated previously identified outcome predictors found in literature in our specific patient cohort. Discrepancies can most likely be accounted for by differences in demographical factors and mortality in other settings. These research findings will assist in the practical usage of readily available laboratory values in predicting outcome in patients with perforated peptic ulcers. It can lead to better clinical decisions and cost-benefit strategies, promote optimal management and facilitate better assignment of resources such as theatre space and consultant coverage. Limited ICU bed availability in most health care settings emphasizes the importance of individual risk stratification. Scoring systems should be easy to calculate and have a high degree of accuracy in predicting adverse outcomes, which have been proven difficult to materialize in this patient group, as seen in the literature. Patients identified as higher risk could have earlier access to organ support, intensive care and more aggressive resuscitation. Outcome can then be improved based on individual risk stratification. It has been proven that extra perioperative care and management protocols for high-risk patients improve 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. Naturally, an individual predictor

can't be ascribed to a single patient, but the presence of a significant or more than one risk factor presents a much higher mortality risk in contrast to patients with none.[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 health care setting or used in different populations as a comparison. Most of the studies available in the literature were done mainly in western and Asian countries.[17] In the era of hand-held devices and smartphones, more complex scoring systems might be easier to calculate at the bedside than before.[23] It might be challenging to develop a universally reproducible scoring system due to geographical variation in age, gender, and presentation patterns.[18] Laboratory values however, have the advantage of being an objective variable not influenced by subjective interpretation and therefore ideal for validation between different patient cohorts and demographic regions.[6]

Although the study involved a consecutive cohort, this study's limitation is that it is a retrospective, single-centre study. An advantage is that we had minimal missing data due to consistent laboratory records, which might be more of a problem in future studies using other perioperative variables depending on pre-hospital and hospital records. Laboratory values might be indicators for other underlying factors like chronic disease. Further investigation into causality from the findings in the study might therefore be warranted at a later stage. Long term outcome after hospital discharge for our patient group was also not assessed. Logical regression was used to minimize confounding variables. Some of the calculated 95 % Confidence intervals are wide, which indicates low statistical precision. Other reference ranges for abnormal values and definitions or categorizations of demographic variables might have produced different results.

Conclusion

All laboratory values might not be exact in predicting mortality, but we found that routine admission laboratory values do most certainly contribute to building a risk stratification model for this patient group in our health care setting. This study simply questioned whether admission laboratory values in isolation could be trusted to assist with predicting outcomes. Even though admission laboratory values cannot be influenced in the same way as other risk factors such as for example time to theatre, they play a crucial role in our approach and management of the patient from the time of admission.

List of abbreviations

ASA	American Society of Anaesthesiologist physical status classification system
CI	Confidence interval
CORES score	Calculation of postoperative risk in emergency surgery
HSREC	Health Science Research Ethics Committee
ICU	Intensive Care Unit
IQR	Interquartile range
Meditech	Medical technology system data storage
NSAIDs	Non-steroidal anti-inflammatory drugs
OR	Odds Ratio
POMPP score	Prediction of mortality in perforated peptic ulcer
PPI	Proton Pump Inhibitor
P-POSSUM score	Portsmouth Physiological and operative severity score for the enumeration of mortality and morbidity (Portsmouth modification of the original POSSUM score)

PPU	Perforated peptic ulcer
PULP score	Peptic Ulcer Perforation score
UFS	University of the Free State
WCC	White Blood Cell Count

Declarations

Ethics approval and consent to participate

Ethical clearance was obtained from the University of the Free State Health Science Research Ethics Committee (HSREC) UFS-HSD2019/0018/2506

Consent for publication

Not applicable

Availability of data and materials

The data that support the findings of this study are available from the Department of Biostatistics, University of the Free State, but restrictions apply to the availability of these data and so are not publicly available. Data are however, available from the authors upon reasonable request and with permission of the Department of Biostatistics, University of the Free

Competing interest

The authors declare that they have no competing interests

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Authors' contributions

WWM was the principal investigator, and wrote the study protocol, performed the data collection, interpreted the results and wrote the manuscript. EAC supervised the study and reviewed the study protocol and the final manuscript. GJ reviewed the study protocol, performed the statistical analysis, assisted with data interpretation and reviewed the manuscript.

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Additional file

Figures

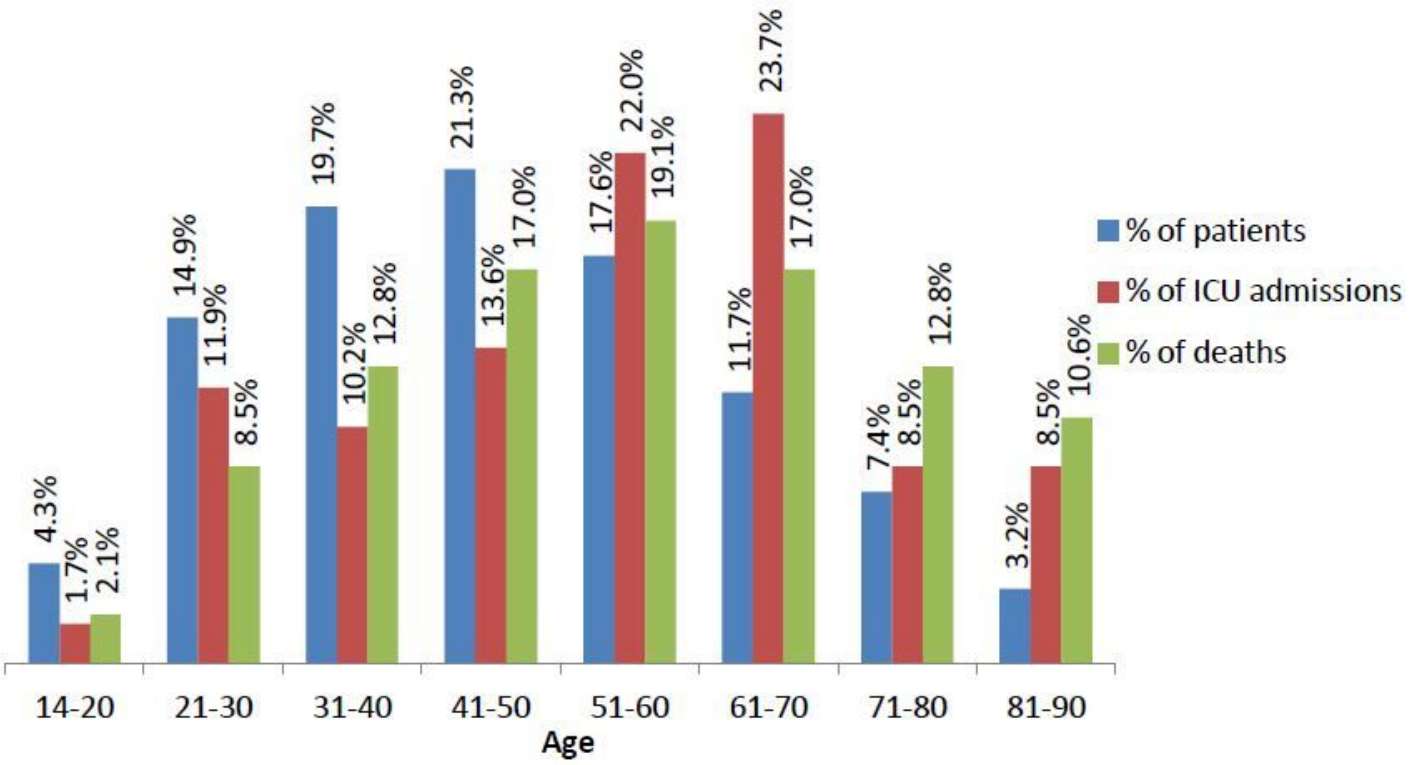

Figure 1

Age, ICU and mortality distribution

Supplementary Files

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