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## Original research

## Neutrophil lymphocyte ratio in outcome prediction after emergency abdominal surgery in the elderly

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## ABSTRACT

**Introduction:** Accurate prediction of outcome after emergency surgery in elderly patients may assist decision-making. Many scoring systems require post-operative data (e.g. P-POSSUM) whilst others have failed to gain widespread use. Recent reports suggest that C-reactive protein (CRP) and the neutrophil lymphocyte (N/L ratio) ratio may predict surgical outcome.

**Methods:** A retrospective review of all patients aged 80 years or over undergoing emergency abdominal surgery over a 22 month period was conducted. Outcome and clinical data were collected. Univariate, multivariate and recursive analyses were performed for outcome at 30 days, 6 months and 12 months. Findings were validated in a second independent dataset.

**Results:** 88 patients were included in the test dataset, median age 84 years. 30-day mortality was 31%, 6-month mortality 43% and 12-month mortality 50%. Univariate analysis identified N/L ratio, CRP, midline laparotomy, and surgical risk score to predict outcome at each time point. Recursive analysis showed, N/L ratio  $\geq 22$  best predicted 30-day outcome ( $p = 0.0018$ ). Multivariate analysis identified N/L ratio to be an independent predictor of 30-day outcome ( $p = 0.004$ ) yet CRP did not predict outcome at any time point. An independent dataset ( $n = 84$ ) confirmed N/L ratio to be a prognostic factor at 30 days ( $p = 0.001$ ), 6 months ( $p < 0.001$ ) and 12 months ( $p = 0.001$ ).

**Conclusion:** N/L ratio is an easily calculable pre-operative measure that may have utility in the prediction of outcome after emergency abdominal surgery in the elderly. Further work to validate this measure in a larger, prospective setting and determine the underlying mechanisms that mediate outcome are necessary.

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## 1. Introduction

An increasing proportion of our population is over 65 years old and forms a large proportion of hospital admissions. The diagnosis and treatment of the elderly brings challenges of providing the highest quality care and maximising quality of life, independence and dignity with the minimum of risk. Many studies have argued that chronological age alone is a poor predictor of outcome after surgery,<sup>1–4</sup> and co-morbidities are of much greater significance.<sup>3,5,6</sup> However, a higher risk is associated with emergency surgery in the elderly,<sup>6–11</sup> and as risk increases the decision to operate becomes increasingly difficult. A number of scoring systems have been developed but are not widely used. APACHE II was devised as

a general measure of severity of disease in intensive care admissions yet does not consider surgical diagnosis and evidence for its role in predicting surgical risk is limited.<sup>12,13</sup> POSSUM and P-POSSUM<sup>14–16</sup> are highly validated surgical scoring systems developed for comparative surgical audit but require operative severity data which limits their pre-operative use and their validity in an elderly population is debated.<sup>17–20</sup> The Surgical Risk Scale<sup>21</sup> (Supplementary Table 1) combines the Confidential Enquiry into Peri-operative Death (CEPOD) rating of the procedure, the British United Provident Association (BUPA) classification of the operative severity and the American Society of Anaesthesiologists (ASA) score of fitness for surgery. This score considers both patient condition and magnitude of surgery and is calculated using clinical data that are available for every patient. Although developed for use in comparative surgical audit it has been shown to have some utility in pre-operative risk prediction in both elective and emergency settings but has failed to gain widespread use.<sup>22,23</sup>

The disadvantages of current outcome prediction scores have led some investigators to assess the utility of novel predictors of

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outcome including C-reactive protein (CRP) and neutrophil/lymphocyte ratio (N/L ratio). The use of CRP in predicting post-operative course may relate to its use as a marker of inflammation and the relationship between pre-operative inflammation and post-operative course,<sup>24,25</sup> yet there remains little evidence for its role in the risk stratification of general surgical patients. More recently the neutrophil/lymphocyte ratio (neutrophil count divided by lymphocyte count, N/L ratio) has been suggested as potentially useful yet few studies have considered the role of neutrophil/lymphocyte ratio in predicting peri-operative outcome. It is suggested that neutrophil/lymphocyte ratio, acting as a surrogate maker of inflammatory response to liver metastases, predicts both overall and disease-free survival,<sup>26</sup> whilst N/L ratio also predicts the severity of clinical course in both medical and post-operative surgical patients in an intensive care unit.<sup>27</sup> The aim of this study is to identify useful predictors of surgical outcome in elderly patients over the age of 80.

## 2. Methods

### 2.1. Data collection

Patients aged 80 years or over undergoing emergency abdominal surgery from May 2005 to February 2007 at a single centre were identified retrospectively from electronic hospital coding systems (Test Dataset). Included were patients undergoing emergency abdominal surgery, appendicectomy, inguinal and femoral hernia repairs. Data were collected on presenting complaint, co-morbidities, routine laboratory investigations including full blood count and C-reactive protein (latest pre-operative results); diagnosis; operative findings and operation performed; post-operative complications, length of intensive care stay, total hospital stay and 30-day mortality. ASA scores were obtained from the anaesthetic records. BUPA and CEPOD categories were classified independently from the available data by two authors (PVS and JR) and any disparity in the scoring resolved after discussion. The categories to which each patient was allocated were converted into a numerical value using the scoring system described by Sutton *et al.*<sup>21</sup>

A second cohort (Validation Dataset) of all patients aged 80 years or over undergoing emergency abdominal surgery at a second centre (university teaching hospital) from October 2008 to April 2010 was also identified retrospectively. Patients were identified from electronic theatre records and data collected from electronic patient records.

### 2.2. Statistical analysis

Data were collated in Excel™ (Microsoft Inc., Seattle, USA) and analysed using Microsoft Excel, Prism 3.03 (GraphPad Software Inc., La Jolla, USA) and SPSS 18.0 (SPSS Inc., Chicago USA). Descriptive statistics were produced using Excel and PRISM. Univariate survival analysis was undertaken using the Kaplan–Meier approach and significant differences identified using the log-rank test. A recursive approach was undertaken to identify the values of N/L ratio that predicted outcome and a K-means cluster analysis performed to confirm the most significant cut-off for N/L ratio. Univariate analysis between the groups 'survived' and 'died' at 3 endpoints was performed to identify significant variables (log-rank  $\chi^2$  test). Variables entered into this model included demographic data, co-morbidity data, laboratory results and ASA, BUPA, CEPOD and SRS scores. Variables with potential to predict outcome ( $p < 0.1$ ) at any temporal endpoint on univariate analysis were included in a multivariate survival model using a Cox regression (stepwise forward model) approach. Variables included were age, malignancy, laparotomy, CEPOD score, BUPA score, ASA score, SRS score, previous TIA, Chronic kidney disease, last pre-operative white cell count, haemoglobin count, neutrophil count, CRP and N/L ratio. N/L lymphocyte ratio was plotted against death rate using a linear regression approach to provide a clinically useful tool for the prediction of outcome. This estimated the death rate at each time point for a given N/L and goodness of fit values ( $R^2$ ) for the model were calculated for 30-day, 6 month and 12 month survival data.

## 3. Results

### 3.1. Patient demographics

The test dataset included 88 patients. Demographics and hospital stay are shown in Table 1. The commonest pre-operative diagnosis was small bowel obstruction and 19 patients had an underlying malignancy. Pre-operative diagnoses and co-morbidities are shown in Supplementary Tables 2 and 3.

**Table 1**

Table showing patient demographics and mean ASA, CEPOD, BUPA and SRS scores together with 30-day, 6-month and 12-month survival for test and validation datasets.

	Test dataset (n = 88)	Validation dataset (n = 84)	p Value
Sex	Male 45 Female 43	Male 34 Female 50	0.2116
Median age (range)	84 (80–95)	84 (80–94)	0.92
Median stay in days (range)	15 (0–72)	17 (0–94)	0.15
Mean CEPOD score (95% CI)	2.94 (2.86–3.03)	3.06 (3.01–3.11)	0.1952
Mean ASA score (95% CI)	2.84 (2.65–3.03)	3.54 (3.41–3.68)	< 0.0001
Mean BUPA score (95% CI)	3.43 (3.29–3.58)	3.82 (3.73–3.92)	< 0.0001
Mean SRS score (95% CI)	9.22 (8.93–9.50)	10.43 (10.26–10.60)	< 0.0001
Mean N/L ratio (95% CI)	12.1 (9.99–14.21)	14.5 (11.34–17.74)	0.47
30 Day mortality (%)	27 (31)	18 (21)	0.13
6 Month mortality (%)	38 (43)	30 (36)	0.40
12 Month mortality (%)	44 (50)	35 (42)	0.23

The mean ASA score was 2.84, with a narrow confidence interval suggesting a consistently high degree of co-morbidity pre-operatively (95% CI 2.65–3.03). CEPOD scoring reflected the emergency nature of the patients with a mean score of 2.94 (95% CI 2.86–3.03), whilst the BUPA operative severity score indicated that the majority of individuals underwent a significant operative intervention (Score 3.43 (95% CI 3.29–3.58); Table 1). The average N/L ratio was 12.1 (range 2.02–58.5; 95% CI 9.99–14.21). The 30-day mortality was 31% ( $n = 27$ ), 6-month mortality 43% ( $n = 38$ ) and 12-month mortality 50% ( $n = 44$ ).

The validation dataset included 84 patients with a median age of 84 years and mean ASA score = 3.54 (95% CI 3.41–3.68). 30-day mortality was 21% ( $n = 18$ ), 6-month mortality was 36% ( $n = 30$ ) and 12-month mortality 42% ( $n = 35$ ).

### 3.2. Univariate survival analysis using previously validated classification tools and patient co-morbidity

Survival was differentiated in the test cohort by ASA score, CEPOD classification and SRS at 30 days, six and twelve months but not by BUPA score (Table 1). Univariate analysis of individual co-morbidities (Supplementary Table 3) revealed that transient ischaemic attack (TIA) and chronic kidney disease (CKD) differentiated outcome ( $p < 0.1$ ) (Table 2).

### 3.3. Identification of predictors of outcome in study group and verification of utility of scoring systems

Midline laparotomy was a significant predictor of outcome at all endpoints ( $p < 0.01$ ), whilst the presence of malignancy did not affect short-term outcome, but did predict survival at 12 months ( $p = 0.02$ ; Tables 2a–c). Variables with predictive significance of  $p < 0.1$  were included in the multivariate analysis. This model identified N/L ratio as an independent prognostic factor at 30 days ( $p = 0.004$ ,  $df = 1$ ,  $\chi^2 = 8.144$ ) but not at 6 or 12 months. CEPOD predicted outcome at 6 months ( $p = 0.001$ ,  $df = 2$ ,  $\chi^2 = 9.16$ ) and 12 months ( $p = 0.001$ ,  $df = 2$ ,  $\chi^2 = 15.04$ ) whilst ASA predicted 12 month outcome alone ( $p < 0.0001$ ,  $df = 8$ ,  $\chi^2 = 43.49$ ). CRP did not predict outcome at any endpoint in this model. Midline laparotomy (when compared to other abdominal incisions) was also an independent predictor of outcome at 30 days ( $p = 0.001$ ,  $df = 2$ ,  $\chi^2 = 15.071$ ), 6 months ( $p < 0.001$ ,  $df = 3$ ,  $\chi^2 = 21.874$ ), and 12 months ( $p < 0.001$ ,  $df = 3$ ,  $\chi^2 = 23.805$ ).

**Table 2a**  
Factors affecting 30-day mortality in test dataset.

	Died ≤30 days	Survived >30 days	Univariate odds ratio (95% CI)	p Value	Multivariate odds ratio (95% CI)	p Value
<i>n</i>	29	59		–		
Male gender	13 (45%)	30 (51%)	1.23 (0.59–2.56)	0.57	–	–
Mean age (95% CI)	85.65 (83.1–85.1)	84.07 (84.3–87.0)	1.07 (0.99–1.16)	0.10	NS	0.11
Malignancy	8 (28%)	11 (19%)	1.35 (0.60–3.05)	0.47	NS	0.21
Previous TIA	5 (17%)	4 (7%)	2.30 (0.88–6.04)	0.08	NS	0.92
Chronic kidney disease	3 (10%)	0 (0%)	4.65 (1.37–15.7)	0.06	NS	0.30
Midline laparotomy	28 (97%)	40 (68%)	10.0 (1.36–73.51)	0.005	8.86 (1.20–65.46)	0.001
Appendectomy	1 (3%)	4 (7%)	0.58 (0.08–4.26)	0.59	–	–
Groin/ventral hernia repair	0	14 (24%)	0.04 (0.001–1.94)	0.009	NS	0.11
Mean CEPOD score (95% CI)	3.10 (3.0–3.3)	2.86 (2.8–3.0)	4.02 (1.61–10.07)	0.006	NS	0.21
Mean ASA score (95% CI)	3.14 (2.8–3.5)	2.69 (2.5–2.9)	1.72 (1.10–2.69)	0.02	NS	0.39
Mean BUPA score (95% CI)	3.62 (3.4–3.9)	3.34 (3.2–3.5)	1.64 (0.99–2.74)	0.06	NS	0.81
Mean SRS score (95% CI)	9.86 (9.4–10.4)	8.90 (8.6–9.2)	1.56 (1.21–2.02)	0.001	NS	0.51
Mean CRP (95% CI)	109.99 (77.3–142.7)	67.67 (43.2–92.2)	1.00 (1.00–1.01)	0.05	NS	0.14
Mean haemoglobin (95% CI)	11.65 (10.8–12.5)	12.69 (12.0–13.4)	0.87 (0.75–1.01)	0.08	NS	0.36
Mean WCC (95% CI)	13.06 (10.9–15.2)	10.70 (9.6–11.9)	1.08 (1.01–1.16)	0.32	NS	0.16
Mean neutrophil count (95% CI)	11.10 (9.0–13.2)	8.81 (7.7–9.9)	1.09 (1.01–1.17)	0.025	NS	0.15
Mean lymphocyte count (95% CI)	0.97 (0.7–1.2)	1.10 (1.0–1.2)	0.67 (0.33–1.38)	0.27	–	–
Mean N/L ratio (95% CI)	16.40 (11.7–21.1)	10.02 (8.1–12.0)	1.04 (1.01–1.07)	0.002	1.03 (1.01–1.06)	0.004

#### 3.4. Survival and recursive analyses of predictors of outcome

Using a recursive approach, an N/L ratio of  $\geq 22$  most significantly differentiated survival in the cohort ( $\chi^2 = 9.784$ ,  $df = 1$ ,  $p = 0.0018$ ; Fig. 1) at 30 days (Supplementary Table 4). A *k*-means cluster analysis ( $k = 2$ ) was subsequently performed and revealed the most significant N/L ratio cut-off to be 22.85.

#### 3.5. Derivation of a model for prediction of outcome

A clinically useful tool for the prediction of outcome modelled N/L lymphocyte ratio against death rate using a linear regression approach (Fig. 2). The model derived had goodness of fit values ( $R^2$ ) of 0.87 for the 30-day survival data, 0.835 for 6 month survival data and 0.692 for the 12 month survival data.

#### 3.6. Validation of model using independent dataset (validation dataset)

Comparison between the test and validation datasets is shown in Table 1. There were no differences in age, N/L ratio, 30-day,

6-month and 12-month mortality but ASA grade, BUPA score and SRS score were higher in test dataset ( $p < 0.0001$ ).

The N/L ratio cut-off of 22.85 derived from the test dataset was applied to the validation dataset using a univariate approach and predicted outcome at 30 days ( $p = 0.0053$ ), 6 months ( $p = 0.0099$ ) and 12 months ( $p = 0.0336$ ; Fig. 3). Multivariate analysis of the validation dataset including the same variables as the test dataset using a forward stepwise Cox regression also showed N/L ratio to be an independent prognostic factor ( $p = 0.001$ ,  $df = 2$ ,  $\chi^2 = 15.071$ ) at 30 days, six months ( $p < 0.001$ ,  $df = 1$ ,  $\chi^2 = 12.536$ ) and 12 months ( $p = 0.001$ ,  $df = 1$ ,  $\chi^2 = 10.27$ ). No other variable independently predicted outcome in this dataset at all three time points.

#### 3.7. Utility analysis and validation of N/L ratio in the validation dataset

Having identified that N/L ratio had prognostic utility when predicting outcome in elderly patients undergoing emergency abdominal surgery we further studied its potential clinical utility through the assessment of predictive accuracy and compared N/L  $\geq 22.85$  against survival at 30 days, 6 months and 12 months in the

**Table 2b**  
Factors affecting 6-month mortality in test dataset.

	Died ≤6 months	Survived >6 months	Univariate odds ratio (95%CI)	p value	Multivariate odds ratio (95%CI)	p value
<i>n</i>	38	50		–	–	–
Male gender	18 (47%)	25 (50%)	1.10 (0.58–2.09)	0.76	–	–
Mean age (95% CI)	85.37 (84.3–86.5)	84.00 (82.8–85.2)	1.06 (0.98–1.14)	0.124	NS	0.15
Malignancy	11 (29%)	8 (16%)	1.52 (0.75–3.06)	0.24	NS	0.08
Previous TIA	6 (16%)	3 (6%)	2.22 (0.93–5.31)	0.07	NS	0.83
Chronic kidney disease	3 (8%)	0	4.65 (1.37–15.70)	0.06	NS	0.67
Midline laparotomy	35 (92%)	33 (66%)	4.47 (1.37–14.54)	0.006	5.84 (1.39–24.53)	<0.0001
Appendectomy	1 (3%)	4 (8%)	0.412 (0.06–3.01)	0.37	NS	0.29
Groin/ventral hernia repair	2 (5%)	12 (24%)	0.22 (0.05–0.92)	0.02	NS	0.45
Mean CEPOD score (95% CI)	2.84 (2.7–2.9)	3.08 (2.9–3.2)	4.11 (1.75–9.64)	0.003	N/A	0.001
Mean ASA score (95% CI)	2.68 (2.5–2.9)	3.05 (2.8–3.4)	1.56 (1.06–2.30)	0.03	NS	0.053
Mean BUPA score (95% CI)	3.34 (3.2–3.5)	3.55 (3.3–3.8)	1.46 (0.93–2.30)	0.10	NS	0.97
Mean SRS score (95% CI)	8.86 (8.5–9.2)	9.68 (9.2–10.2)	1.48 (1.17–1.86)	0.001	NS	0.90
Mean CRP (95% CI)	91.69 (63.6–119.8)	74.79 (46.8–102.8)	1.00 (1.00–1.01)	0.27	NS	0.12
Mean haemoglobin (95% CI)	11.92 (11.1–12.8)	12.68 (12.1–13.3)	0.90 (0.79–1.03)	0.13	NS	0.53
Mean WCC (95% CI)	12.31 (10.68–14.0)	10.85 (9.5–12.2)	1.05 (0.99–1.12)	0.11	NS	0.08
Mean neutrophil count (95% CI)	10.32 (8.7–12.0)	8.99 (7.8–10.2)	1.06 (0.99–1.13)	0.11	NS	0.06
Mean lymphocyte count (95% CI)	1.06 (0.9–1.3)	1.06 (0.9–1.2)	0.90 (0.50–1.60)	0.71	–	–
Mean N/L ratio (95% CI)	14.01 (10.1–17.9)	10.69 (8.5–12.9)	1.03 (1.00–1.06)	0.034	NS	0.31

**Table 2c**  
Factors affecting 12-month mortality in test dataset.

	Died ≤12 months	Survived >12 months	Univariate odds ratio (95%CI)	p value	Multivariate odds ratio (95%CI)	p value
<i>n</i>	44	44	–	–	–	–
Male gender	22 (50%)	21 (48%)	0.97 (0.54–1.76)	0.93	–	–
Mean age (95% CI)	85.71 (84.6–86.0)	83.48 (82.4–84.6)	1.08 (1.02–1.15)	0.01	1.09 (1.02–1.17)	<0.0001
Malignancy	15 (34%)	4 (9%)	2.06 (1.10–3.86)	0.02	2.62 (1.25–5.49)	<0.0001
Previous TIA	6 (14%)	3 (7%)	1.97 (0.83–4.67)	0.12	NS	0.17
Chronic kidney disease	3 (7%)	0	4.65 (1.38–15.68)	0.006	NS	0.47
Midline laparotomy	40 (91%)	28 (64%)	4.01 (1.43–11.24)	0.004	5.06 (1.17–21.85)	<0.0001
Appendectomy	2 (5%)	3 (7%)	0.70 (0.17–2.88)	0.62	NS	0.18
Groin/ventral hernia repair	2 (5%)	12 (27%)	0.18 (0.5–0.76)	0.009	NS	0.57
Mean CEPOD score (95% CI)	3.02 (2.9–3.2)	2.86 (2.8–3.0)	2.96 (1.25–7.01)	0.02	N/A	0.001
Mean ASA score (95% CI)	3.00 (2.7–3.3)	2.68 (2.4–2.9)	1.48 (1.03–2.13)	0.03	NS	0.47
Mean BUPA score (95% CI)	3.52 (3.3–3.7)	3.34 (3.2–3.5)	1.39 (0.91–2.14)	0.13	NS	0.87
Mean SRS score (95% CI)	9.55 (9.1–10.0)	8.89 (8.5–9.3)	1.41 (1.12–1.76)	0.003	NS	0.68
Mean CRP (95% CI)	94.03 (67.1–121.0)	70.85 (41.6–100.1)	1.00 (1.00–1.01)	0.19	NS	0.61
Mean haemoglobin (95% CI)	11.98 (11.2–12.8)	12.72 (12.0–13.4)	0.91 (0.81–1.03)	0.13	NS	0.81
Mean WCC (95% CI)	12.53 (11.0–14.1)	10.43 (9.1–11.8)	1.06 (1.00–1.13)	0.04	NS	0.87
Mean neutrophil count (95% CI)	10.50 (9.0–12.0)	8.62 (7.3–9.9)	1.07 (1.00–1.14)	0.04	1.09 (1.01–1.16)	<0.0001
Mean lymphocyte count (95% CI)	1.09 (0.9–1.3)	1.03 (0.8–1.2)	1.00 (0.60–1.68)	0.99	–	–
Mean N/L ratio (95% CI)	13.56 (10.1–17.0)	10.69 (8.3–13.1)	1.03 (1.00–1.05)	0.04	NS	0.72

NS Non-significant.

N/A overall odds ratio not available for categorical variables.

Validation Dataset. The specificity of N/L ratio at this cut-off was calculated and shown to be moderately high at 30 days (88%), 6 months (89%) and 12 months (88%) (Table 3). Negative predictive value at 30 days was 84% (95%CI 74–91) and positive predictive value 47% (95%CI 25–70). N/L ratio has a good overall accuracy in the early period after surgery (30 days; 77%) but became increasingly inaccurate at 6 months (68%) and 12 months (62%).

**4. Discussion**

Accurate prediction of outcome after emergency surgery, particularly in the elderly, would be advantageous, assisting clinicians when discussing early morbidity and mortality with patients and their families and guiding difficult treatment decisions. The

need for improved methods to predict short-term clinical outcomes in these patients is highlighted by the 50% 12 month mortality in the recruited patients.

Many outcome prediction models have been suggested although none specific to the elderly patient.<sup>28</sup> Furthermore certain scoring tools require operative information e.g. POSSUM<sup>15</sup> and therefore cannot be easily used in the pre-operative period. In our test dataset both ASA and CEPOD scoring predicted mortality suggesting that data from our cohort, even considering individual patient variation, were generalisable in terms of outcome. CRP, however, was not an independent predictor of outcome.

Three recent reports suggest that N/L ratio may predict outcome after resection of colorectal carcinoma,<sup>29</sup> colorectal liver metastases,<sup>26</sup> and in critically unwell individuals in an intensive care

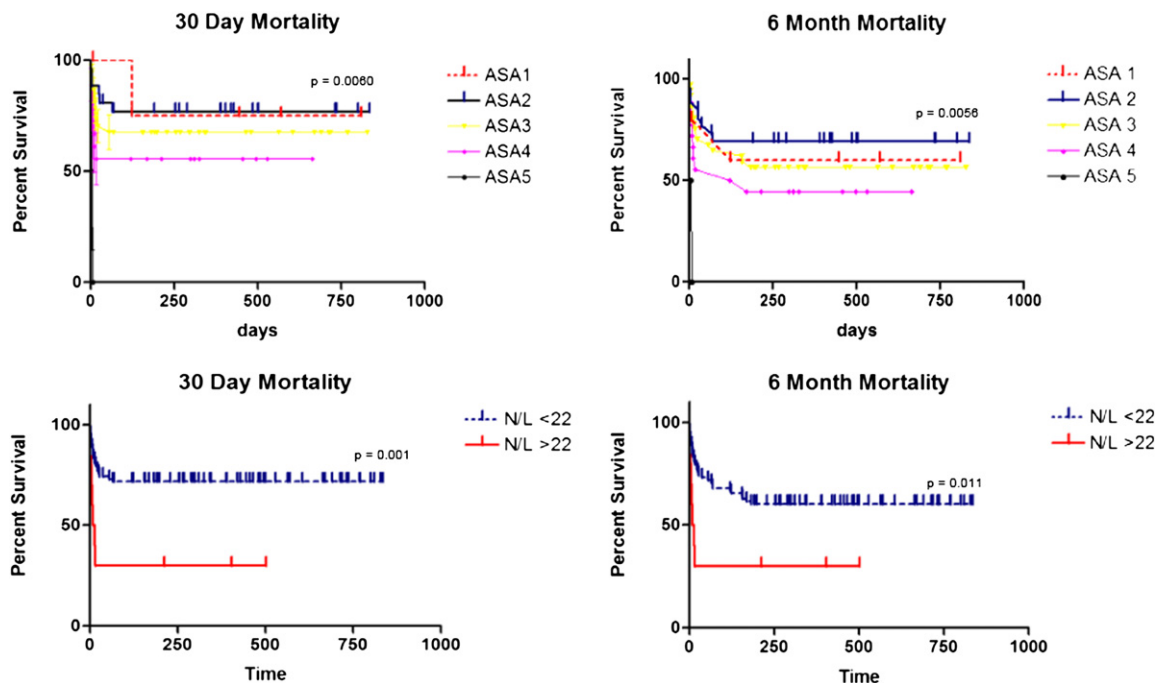


Fig. 1. Kaplan–Meier survival curves for ASA scores and N/L ratio ≥22 in test dataset, p values calculated using log-rank approach.

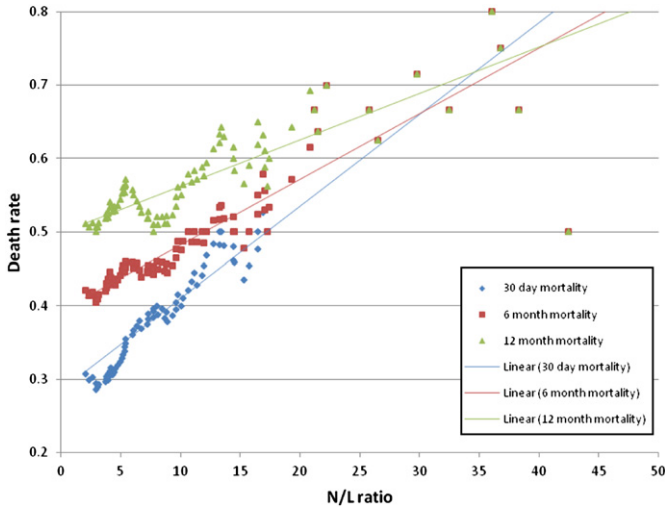


Fig. 2. Graph describing death rate against N/L ratio in test dataset with line of best fit plotted.

setting.<sup>27</sup> In the test dataset N/L ratio was an independent predictor of outcome on multivariate analysis ( $p = 0.004$ ,  $df = 1$ ,  $\chi^2 = 8.144$ ) suggesting potential clinical utility. A recursive approach showed that an N/L ratio of  $\geq 22.85$  best differentiated survival in the cohort

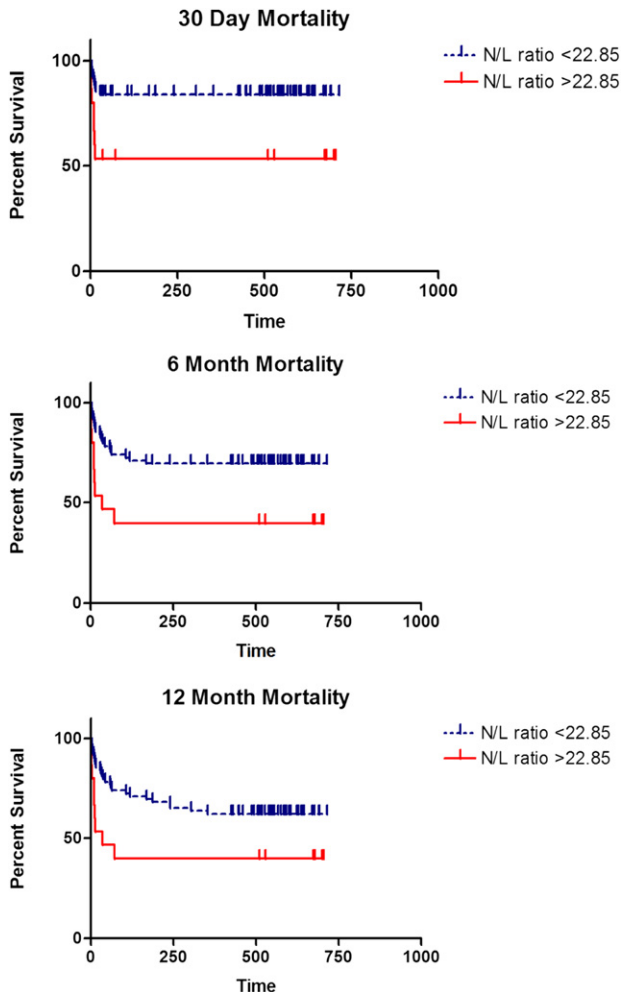


Fig. 3. Kaplan–Meier survival curves for N/L ratio  $\geq 22.85$  in test dataset,  $p$  values calculated using log-rank approach.

Table 3

Sensitivity and specificity of neutrophil/lymphocyte (N/L) ratio  $\geq 22.85$  and laparotomy in validation dataset.

	N/L ratio $\geq 22.85$	30 Day mortality	6 Month mortality	12 Month mortality
Sensitivity	39% (95%CI 18–64)	30% (95%CI 15–50)	26% (95%CI 13–44)	
Specificity	88% (95%CI 77–94)	89% (95%CI 77–95)	88% (95%CI 75–95)	
<b>Laparotomy</b>				
Sensitivity	94% (95%CI 71–100)	93% (95%CI 76–99)	89% (95%CI 72–96)	
Specificity	14% (95%CI 7–25)	15% (95%CI 7–28)	12% (95%CI 5–25)	
<b>N/L ratio <math>\geq 22.85</math> and laparotomy</b>				
Sensitivity	39% (95%CI 18–64)	30% (95%CI 26–47)	26% (95%CI 13–44)	
Specificity	89% (95%CI 79–95)	91% (95%CI 79–97)	90% (95%CI 77–96)	

at 30 days, 6 months and 12 months. This cut-off was validated using a *K*-means approach to overcome the limitations of recursive analysis. To validate the utility of N/L ratio in this setting we undertook the analysis in a second independent cohort (Validation Dataset) which confirmed N/L ratio to be an independent prognostic marker at 30 days, but also at 6 months and 12 months.

To further investigate N/L ratio utility as a prognostic tool we demonstrated that it had a moderately high specificity (88%) and a high accuracy (77%) at 30 days. The negative predictive value was 84% showing that patients with a low ratio were likely to survive. However, positive predictive value was only 47% indicating that a high N/L ratio does not necessarily predict a poor outcome.

Lymphopaenia and neutrophilia were commonly present in patients who did not survive in both datasets. Whilst surgeons often look for neutrophilia when determining whether a patient has severe sepsis they rarely examine the lymphocyte count. Further work is required to understand why this cohort of severely unwell elderly patients had lymphopaenia and how this contributed to their outcome. In addition, further investigation to determine whether lymphopaenia is a response to severe sepsis through lymphocyte apoptosis,<sup>30</sup> or whether lymphopaenia characterises an elderly group with an impaired immune system are required.<sup>31</sup> The role of N/L ratio in predicting outcome in those under 80 years of age also requires investigation.

This study had a number of limitations. Data were collected retrospectively introducing the potential for selection bias. Secondly risk prediction and outcome from a holistic standpoint together with assessment of patient-reported outcomes are necessary. The ability to conduct activities of daily living may indicate good pre-morbid condition, while post-operative discharge to a fully dependent existence in a nursing home may indicate a poor outcome not identified by traditional markers of morbidity or mortality. Indeed, health related quality of life indicators, such as physical functioning, have been demonstrated to have prognostic utility in a meta-analysis of clinical trials.<sup>32</sup> Holistic factors should not be overlooked and must be considered in the decision-making process and in discussions with patients and relatives.

5. Conclusions

The study demonstrates a high level of mortality following emergency abdominal surgery in the elderly while analysis identifies N/L ratio as an independent predictor of outcome in this cohort. N/L ratio of  $< 22.85$  or  $\geq 22.85$  was most discriminatory for survival. The value of this marker was validated in an independent dataset and performs with good specificity and accuracy. Prospective evaluation of these findings in a larger cohort to assess its clinical effectiveness is necessary together with further studies to determine the biological rationale for these findings.

**Conflict of interest**

None declared.

**Funding**

None declared.

**Ethical approval**

None declared.

**Author contribution**

PV-S – Study design, data collection and writing.

JR – Study design, data-analysis and writing.

AK – Data-analysis and writing.

**Appendix. Supplementary material**

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ijso.2012.02.010.

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