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A single-centre cohort study of National Early Warning Score (NEWS) and near patient testing in acute medical admissions

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Abstract

Introduction: The utility of an early warning score may be improved when used with near patient testing. However, this has not yet been investigated for National Early Warning Score (NEWS). We hypothesised that the combination of NEWS and blood gas variables (lactate, glucose or base-excess) was more strongly associated with clinical outcome compared to NEWS alone.

Methods: This was a prospective cohort study of adult medical admissions to a single-centre over 20-days. Blood gas results and physiological observations were recorded at admission. NEWS was calculated retrospectively and combined with the biomarkers in multivariable logistic regression models. The primary outcome was a composite of mortality or critical care escalation within 2 days of hospital admission. The secondary outcome was hospital length of stay.

Results: After accounting for missing data, 15 patients out of 322 (4.7%) died or were escalated to the critical care unit. The median length of stay was 4 (IQR 7) days. When combined with lactate or base excess, NEWS was associated with the primary outcome (OR 1.18, p=0.01 and OR 1.13, p=0.03). However, NEWS alone was more strongly associated with the primary outcome measure (OR 1.46, p<0.01). The combination of NEWS with glucose was not associated with the primary outcome. Neither NEWS nor any combination of NEWS and a biomarker were associated with hospital length of stay.

Conclusion: Admission NEWS is more strongly associated with death or critical care unit admission within 2 days of hospital admission, compared to combinations of NEWS and blood-gas derived biomarkers.

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1. Introduction

Predicting clinical outcomes in acutely unwell patients can be challenging. Early warning scores (EWS) are often used to identify patients who may benefit from an escalation of care. In the United Kingdom, the National Early Warning Score (NEWS) is becoming universal [1, 2]. ENREF 3 NEWS weights various physiological measurements by severity (table 1) and the results are combined to give a composite score, which reflects how unwell the patient is [3]. EWS, like NEWS, have the potential to improve risk assessment in acutely unwell patients. NEWS is associated with admission to a critical care unit (level two or three care) and death in studies of patients with cancer, sepsis and medical diagnoses [4-8]. However, there is wider scope for using EWS as tools for prognostication in acutely unwell patients.

Table 1.

National Early Warning Score (NEWS)							
	3	2	1	0	1	2	3
Temperature (°C)	<35.0		35.1-36.0	36.1-38.0	38.1-39.0	>39.0	
Heart rate (beats/min)	<41		41-50	51-90	91-110	111-130	>130
Systolic BP (mmHg)	<91	91-100	101-110	111-219			>219
Respiratory Rate (breaths/min)	<9		9-11	12-20		21-24	>25
Oxygen Saturation (%)	<92	92-93	94-95	>96			
Supplemental oxygen		Yes		No			
CNS response (AVPU)				A			V, P, U

Each category is graded 0-3. Scores for each category are added together to give a total. Composite scores of greater than 5 (or 3 in any one parameter) trigger an urgent medical review. A score of over 7 triggers a review by a critical care outreach team or medical response team.[5, 6]

Near patient testing on admission to hospital, for example arterial or venous blood gas sampling, is increasingly common and some blood gas variables are associated with clinical outcome [9]. In the literature there are established correlations between poor prognosis and elevations in serum lactate or acid base derangement in critically ill patients, as well as raised serum glucose following myocardial infarction. [10-14]. The combination of EWS with near patient testing offers the exciting prospect of

improving risk stratification in acute medical patients. Limited evidence suggests that the addition of serum lactate to EWS improved association with clinical outcome, compared to EWS alone [15]. However, it is unknown whether lactate or other blood gas variables could improve the utility of NEWS, in predicting clinical outcome [15].

We aim to determine whether combinations of NEWS and three blood gas variables (lactate, glucose and base-excess) on admission to hospital are associated with mortality or critical care unit (level two or three care) escalation within the first 48 hours of hospital admission. We hypothesise that NEWS combined with any of the blood gas variables is more strongly associated with outcome compared to NEWS alone.

2. Method

2.1 Study design

This was a planned secondary analysis of a prospective observational cohort study of undifferentiated adult medical ward patients. We have previously described the study design and data collection in detail [4]. Patients were identified for inclusion from the acute medical take list. We included all new unplanned medical admissions to the acute admissions unit at a large teaching hospital, during a 20-day period between 25th March and 13th April 2013. Patients that were not admitted via the acute admissions unit were not included in the study, for example direct admissions to speciality wards for planned inpatient care and patients admitted directly to the critical care unit from the emergency department. The study protocol was reviewed and approved by the National Research Ethics Service (12/LO/1985).

2.2 Outcome measures

The primary outcome was a composite of mortality and critical care unit (level two or three care) escalation within the first 48 hours of hospital admission. This captured all patients with cardiac arrest at our institution, since all cardiac arrest survivors are admitted to the critical care unit. This outcome measure has been used previously in similar studies [4-6, 16]. The secondary outcome measure was hospital length of stay.

2.3 Data collection

Clinical staff recorded physiological observations on the bedside observation chart when patients were first admitted to a medical ward. Near patient testing is routinely used at our institution and the majority of patients have either a venous or arterial blood gas measurement as part of their routine medical clerking. Samples were

analysed using an ABL 500 Flex (Diamond Diagnostics, USA) machine. Researchers recorded the first set of observations after admission and the first blood gas measurement of lactate, glucose and base excess. If any of these variables were not available within 24 hours of admission, they were considered missing for the purpose of our analysis. Data were transcribed from paper pro-formas to an electronic database, which was independently checked at random to ensure the accuracy of data entry. Patient records and discharge summaries were reviewed to assess the outcomes. Admission NEWS was calculated using Microsoft Excel (Microsoft Inc., Redmond WA).

2.4 Selection of blood gas variables

We selected the blood gas variables prospectively before starting data collection. Our choice was pragmatic in order to balance data quantity and quality against the ease of data collection. Therefore we chose a small number of variables that we expected to have a high diagnostic yield. Lactate has previously been investigated in similar studies, while glucose and base excess are often deranged in acute illness.[9, 13-15]

2.5 Statistical analysis

Data were analysed using SPSS version 21 (IBM, Armonk, NY). NEWS, lactate, glucose and base excess were considered as continuous variables. We first assessed for association between the independent variables (NEWS, lactate, glucose and base excess) and the primary outcome measure using logistic regression analysis. We first used univariable (unadjusted) regression and then corrected the analysis for age and gender, using multivariable logistic regression analysis, to facilitate comparison with other research in this field [5, 6]. To determine if the addition of age or gender

influenced the strength of association with the primary outcome, we compared the results of the adjusted and unadjusted models. To determine which of NEWS, lactate, glucose or base excess was the stronger predictor of the primary outcome we compared the odds ratios.

Previous research combined lactate and an early warning score by adding the absolute values of the early warning score and lactate to create a composite score that was predictive of clinical outcome.[15] We used this approach to create a set of composite scores by adding the absolute values of admission NEWS to each of lactate, glucose or base excess. To determine whether these composite scores were associated with the primary outcome we repeated the regression analyses using these variables. To determine if the composite scores were more strongly associated with the primary outcome than NEWS alone, we compared the results of the regression models. We calculated Hosmer-Lemshow statistics as a measure goodness of fit for each model. We repeated these analyses for the secondary outcome measure using linear regression, as length of stay is a continuous variable.

2.6 Post-hoc sensitivity analyses

In order to compare the predictive accuracy of NEWS with the composite scores defined above, we constructed receiver operating characteristic curves and calculated the area under these (AUROC). We considered predictive ability in standard terms, where AUROC of 0.6-0.7 is poor, AUROC of 0.7-0.8 is fair, AUROC of 0.8-0.9 is good and AUROC >0.9 is excellent.[17] We were interested to know if an alternative method of combining NEWS with the blood gas variables would yield an improvement in the association of the composite score with the primary outcome

measure. We recalculated the composite score for lactate by combining various weightings of lactate and NEWS together and then repeating the primary analysis. To take account of patients that died, we repeated the length of stay analysis having removed cases that died.
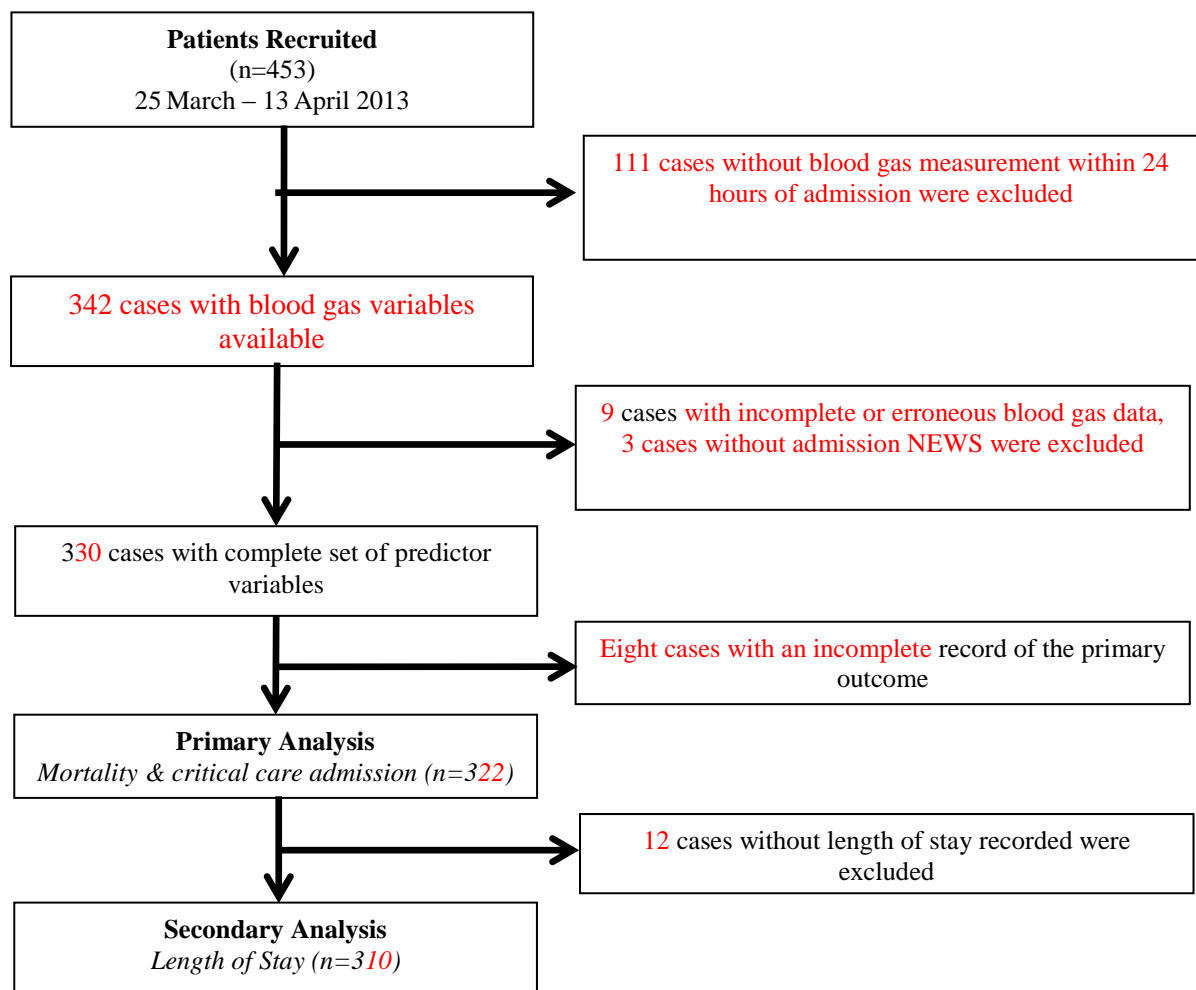

Figure 1. Flow diagram of cases included in the analysis

3. Results

Data from 453 patients were available. Cases with missing predictors were excluded from the analysis, as well as eight patients with an ambiguous record of the primary outcome, leaving 322 cases in the primary analysis and 310 cases in the secondary analysis (figure 1). Demographic data for the cases without blood gas data are provided in supplemental table 1. Of the cases included in the primary analysis, 33 (10.2%) blood gas samples were arterial, 285 (88.5%) were venous and 4 (1.2%) were not recorded as either venous or arterial. 15 patients (4.7%) died or were escalated to the critical care unit within 48 hours of hospital admission. The median length of hospital stay was 4 (IQR 7) days. Demographic data and the main diagnosis categories for patients included in this analysis are shown in table 2.

Table 2.

Patient demographics and diagnosis groups	Whole cohort	NEWS $\geq$ 5
Frequency	322	54
Age in years (sd)	63.0 (21.8)	63.5 (23.1)
Male	153 (47.5)	32 (58.2)
Admission NEWS (IQR)	2 (2.0)	6 (2.0)
Blood gas variables (sd)		
Lactate	1.9 (1.9)	1.9 (1.1)
Glucose	8.1 (4.8)	8.0 (3.9)
Base excess (absolute values)	2.7 (2.7)	2.3 (2.0)
Post-take Diagnosis Category		
General Medical	94 (29)	12 (22)
Health Care of the Elderly	89 (28)	13 (25)
Respiratory	56 (17)	19 (35)
Cardiology	34 (10)	7 (13)
Neurological	16 (5)	-
Gastroenterology	11 (3)	1 (2)
Endocrinology	10 (3)	-
Haematology	5 (2)	1 (2)
Oncology	6 (2)	1 (2)
Other	2 (1)	-

Table 3.

Association between admission NEWS, blood gas variables and the primary outcome (critical care escalation or death within 48 hours of hospital admission).

	Odds Ratio	p-value	H-L	p-value
Univariable logistic regression without adjustment for covariates				
NEWS	1.48	<0.01	3.73	0.59
Lactate	1.06	0.56	15.53	0.03
Glucose	0.84	0.19	9.62	0.29
Base excess	1.02	0.85	5.83	0.67
Multivariable logistic regression with adjustment for age and gender				
NEWS	1.46	<0.01	5.59	0.69
Age	1.01	0.59		
Gender	1.46	0.50		
Lactate	1.05	0.62	9.05	0.34
Age	1.01	0.53		
Gender	1.61	0.38		
Glucose	0.85	0.18	3.74	0.88
Age	1.01	0.45		
Gender	1.75	0.30		
Base excess	1.02	0.86	12.89	0.12
Age	1.01	0.54		
Gender	1.65	0.35		

Logistic regression analysis, showing unadjusted odds ratios (univariable analysis) and then separate multivariable models adjusting each variable for age and gender. Hosmer-Lemeshow (H-L) statistics for goodness of fit are presented with corresponding p-values.

We constructed univariable and multivariable logistic regression models of NEWS, lactate, base excess and glucose against the primary outcome variable (Table 3). Hosmer-Lemeshow statistics suggest that the statistical models are well fitting. The results illustrate that NEWS was associated with death or critical care admission (OR

1.46, p<0.01), as previously reported.[6] However, the three blood gas variables did not show a significant association with the primary outcome measure in either the univariable or multivariable models. To further explore this, we repeated these analyses treating the blood gas variables as categorical variables corrected for age and gender. However, none were associated with the primary outcome (supplementary table 2). To investigate combinations of NEWS and blood gas variables, we constructed logistic regression models using dummy variables consisting of the numerical sum of NEWS and each of the biomarkers (Table 4). From these models NEWS + lactate and NEWS + base excess showed significant association with the primary outcome measure (OR 1.18, p=0.01 and OR 1.13, p=0.03). However, these composite variables were less strongly associated with the primary outcome measure compared to NEWS alone.

Table 4.

Association between the sum of NEWS and biomarkers, with primary outcome measure (critical care admission or death within 48 hours).

	Odds Ratio	p-value	H-L	p-value
Univariable logistic regression without adjustment for covariates				
NEWS	1.48	<0.01	3.73	0.59
NEWS + Lactate	1.19	<0.01	8.02	0.43
NEWS + Glucose	1.02	0.62	3.56	0.89
NEWS + Base excess	1.13	0.02	3.73	0.88
Multivariable logistic regression with adjustment for age and gender				
NEWS	1.46	<0.01	5.59	0.69
Age	1.01	0.59		
Gender	1.46	0.50		
NEWS + Lactate	1.18	0.01	5.46	0.71
Age	1.01	0.52		
Gender	1.37	0.57		
NEWS + Glucose	1.02	0.70	13.70	0.09
Age	1.01	0.54		
Gender	1.62	0.37		

NEWS + Base excess	1.13	0.03	6.04	0.46
Age	1.01	0.57		
Gender	1.56	0.42		

Logistic regression analysis showing unadjusted odds ratios (univariable analysis) and adjusted odds ratios for combinations of NEWS and blood gas derived biomarkers. Hosmer-Lemeshow (H-L) statistic for goodness of fit is presented with p-values.

NEWS was not associated with hospital length of stay (r^2= 3.5, p= 0.33). The addition of blood gas variables to the linear regression model did not improve the model fit. The composite predictors of NEWS and the blood gas variables were not associated with length of stay (table 5). When patients that died were excluded from the length of stay analysis, the results were unchanged (supplementary table 4).

Table 5.

Association between early warning score and the secondary outcome measure (hospital length of stay)

	r-squared	p-value
Univariable linear regression without adjustment for covariates		
NEWS	0.3%	0.30
Lactate	0.3%	0.38
Glucose	0.8%	0.11
Base excess	0.1%	0.66
NEWS + Lactate	0.0%	0.88
NEWS + Glucose	0.4%	0.29
NEWS + Base excess	0.3%	0.33
Multivariable linear regression with adjustment for age and gender		
NEWS	3.5%	0.33
Age		<0.01
Gender		0.62
NEWS + Lactate	3.2%	0.85
Age		<0.01
Gender		0.63
NEWS + Glucose	3.6%	0.27
Age		<0.01
Gender		0.72
NEWS + Base excess	3.4%	0.40

Age	<0.01
Gender	0.63

Linear regression analysis, showing unadjusted analysis and then separate multivariable models adjusting each variable for age and gender.

We conducted a post-hoc area under receiver operator characteristic curve (AUROC) analysis to test the predictive ability of NEWS and the blood gas derived variables for the primary outcome. NEWS was a poor predictor of critical care unit admission or death (AUROC 0.68, p<0.01), while blood gas variables were very poor predictors of critical care unit admission or death (Lactate: AUROC 0.54, p=0.54; Glucose: AUROC 0.37, p=0.04; Base excess: AUROC 0.48, p=0.69). The ROC curves are presented in the supplementary file. We conducted a further post-hoc analysis to investigate an alternative method for combing NEWS and lactate. We derived a series of composite variables by combining NEWS and lactate in differential proportions (1.00/0.00, 0.75/0.25, 0.667/0.333, 0.5/0.5, 0.333/0.667, 0.25/0.75, 0.00/1.00) and then repeating the primary analysis. We found that when the weighting of the composite remained in favour of NEWS the covariate was significantly associated with the primary outcome (p<0.01). However, as the weighting moved from an equal proportion to being in favour of lactate, the association ceased to be statistically significant (p=0.05 – p=0.56). The full results are shown in supplementary table 3.

4. Discussion

Our principal finding is that composite variables combining NEWS with either lactate or base excess were associated with death or critical care unit escalation within 48 hours of hospital admission. However, NEWS alone was more strongly associated with this outcome. We did not identify associations between any combination of NEWS and blood gas variables with hospital length of stay. This supports our other published work, which suggests that NEWS is a poor predictor of hospital length of stay [4], but contrasts with other EWS where a relationship as been noted.[18] This could reflect differences between early warning scores or the populations under investigation.

We did not identify association between lactate and clinical outcome [15, 19]. We considered lactate as a continuous variable, but we also repeated the analysis using categorical values (<2.5, 2.5-4.0 and >4.0mmol/L) and our results were unchanged. This contrasts with other studies, which were largely restricted to homogeneous patient groups with sepsis or critical illness [10, 12]. In our study, the combination of NEWS and lactate was associated with the primary outcome. However, when we examined differential weighting of NEWS and lactate as part of a composite predictor, our results suggest that the observed association is predominantly due to NEWS and not lactate. We did not find an association between hyper/hypo-glycaemia and clinical outcome. In contrast to studies of surgical patients or those with myocardial infarction, which identify hyperglycaemia as a poor prognostic indicator [20, 21]. Our results may be explained by reduced severity of illness or greater heterogeneity of cases in our sample compared to previous cohorts, or alternatively,

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the modest incidence of the primary outcome measure (4.4%). Whilst our sample size was more than twice as large as the only other study of this type, our event rate was lower [15]. Nonetheless, our statistical methods are appropriate for the event rate and sample size.

This is the first study, of which we are aware, to investigate the combination of NEWS with near patient testing. One study combined point-of-care lactate measurement in critical care unit patients with ViEWS to create ViEWS-L, finding that ViEWS-L had better predictive accuracy when compared to ViEWS alone. However, the methods, which use both simple addition and multivariable logistic regression modelling to create composite scores, are unclear [15]. To take account of the uncertainty in their methodology, we tested both approaches to combine NEWS and the three chosen biomarkers. However, neither method increased the strength of association of NEWS with either outcome measure. Our data do not support using blood gas variables, either alone or in combination with NEWS, for risk stratification. This directly contrasts with previous work and casts doubt over the benefit of combing EWS with blood gases.

This study has several limitations. The analysis was prospectively designed to test NEWS in a ward environment opposed to the emergency department, where much research has already been conducted [6, 15, 22-24]. Therefore patients admitted to the critical care unit directly from the emergency department were not included and our sample represents patients who were initially suitable for ward-based care. Our sample represents a broad spectrum of medical presentations. However, there may be unidentified trends or common characteristics within our sample. We are not aware of

any local factors during the study period that could influence the results, such as major incidents.

We did not perform blood gas testing as part of the study protocol; instead the proportion of patients with a blood gas measurement reflects routine clinical practice at our institution. Patients that received blood gas testing tended to be older and have a higher admission NEWS, suggesting they were more acutely unwell compared to patients without blood gas testing. We excluded patients without a blood gas measurement (figure 1) from the analysis. This may represent a form of selection bias, since the decision not to take a blood gas sample may be influenced by a variety of clinical or non-clinical factors. Unfortunately, we were constrained by the data available as part of routine care, but if we repeated this study we would mandate prospective point of care blood gas testing as part of the protocol. Our choice of blood gas variables was a pragmatic decision. We chose a small number of variables that we expected to have a high diagnostic yield. Lactate has previously been investigated in similar studies, while glucose and base excess are often deranged in acute illness. In the statistical analysis, we did not differentiate between venous or arterial blood-gas sampling [15, 25, 26]. However, we acknowledge that arterial and venous lactate measurement may differ in very abnormal samples [9]. We performed a sensitivity analysis the using type of blood gas sample as a covariate in the multivariable model, and the results did not alter our original conclusions.

5. Conclusion

The combination of admission NEWS and either lactate or base excess is associated with death or critical care unit escalation within 48 hours of hospital admission. But, NEWS alone was more strongly associated with this outcome measure. This research represents the first study to examine the relationship between combinations of NEWS and near patient testing, and clinical outcomes in medical ward patients. Our results sit in contrast with previous work in this field and, as such, should be interpreted with caution. Biomarkers may represent a potential method of risk stratifying acute medical patients at the point of admission to hospital. However, we further research in multi-cohort cohorts is recommended.

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