Glucose as an additional parameter to National Early Warning Score (NEWS) in prehospital setting enhances identification of patients at risk of death: an observational cohort study

Hanna Vihonen ,[1,2] Mitja Lääperi,[2] Markku Kuisma,[2] Jussi Pirneskoski,[2] Jouni Nurmi[2]

[1]Department of Emergency Medicine and Services, Päijät-Häme Central Hospital, Lahti, Finland
[2]Department of Emergency Medicine and Services, Helsinki University and Helsinki University Hospital, Helsinki, Finland

Correspondence to
Dr Hanna Vihonen, Department of Emergency Medicine and Services, Päijät-Häme Central Hospital, Lahti, Finland; hanna.vihonen@phsotey.fi

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ABSTRACT

Background To determine if prehospital blood glucose could be added to National Early Warning Score (NEWS) for improved identification of risk of short-term mortality.

Methods Retrospective observational study (2008–2015) of adult patients seen by emergency medical services in Helsinki metropolitan area for whom all variables for calculation of NEWS and a blood glucose value were available. Survival of 24 hours and 30 days were determined. The NEWS parameters and glucose were tested by multivariate logistic regression model. Based on ORs we formed NEWSgluc model with hypoglycaemia (≤3.0 mmol/L) 3, normoglycaemia 0 and hyperglycaemia (≥11.1 mmol/L) 1 points. The scores from NEWS and NEWSgluc were compared using discrimination (area under the curve), calibration (Hosmer-Lemeshow test), likelihood ratio tests and reclassification (continuous net reclassification index (cNRI)).

Results Data of 27 141 patients were included in the study. Multivariable regression model for NEWSgluc parameters revealed a strong association with glucose disturbances and 24-hour and 30-day mortality. Likelihood ratios (LRs) for mortality at 24 hours using a cut-off point of 15 were for NEWSgluc: LR+ 17.78 and LR− 0.96 and for NEWS: LR+ 13.50 and LR− 0.92. Results were similar at 30 days. Risks per score point estimation and calibration model showed glucose added benefit to NEWS at 24 hours and at 30 days. Although areas under the curve were similar, reclassification test (cNRI) showed overall improvement of classification of survivors and non-survivors at 24 days and 30 days with NEWSgluc.

Conclusions Including glucose in NEWS in the prehospital setting seems to improve identification of patients at risk of death.

Key messages

What is already known on this subject

- The National Early Warning Score (NEWS) is a widely used, although not yet optimal, scoring tool to discriminate critical illness that is used in both the hospital and, more recently, prehospital settings. Blood glucose disturbance is a common phenomenon during critical illness, can be quickly detected in the prehospital setting and could therefore be helpful in improving the accuracy of NEWS.

What this study adds

- In this retrospective study of 27 141 prehospital transfers, addition of blood glucose improved the ability of NEWS to enhance identification of patients at risk of death.

INTRODUCTION

Identifying critically ill patients as early as possible facilitates better care.[1] The National Early Warning Score (NEWS) can help predict which patients are at risk for critical illness using simple commonly measured parameters: BP, HR, respiratory rate, blood oxygen saturation, temperature and level of consciousness. Although NEWS may still miss people at increased risk of death, it is thus far the best and most widely used scoring tool to screen critically ill patients.[2] Initially, NEWS was implemented in the hospital setting but has recently been adopted to emergency medical services (EMS) as well.[3]

During acute illness, blood glucose homeostasis is often disturbed. As a result, a condition called stress-induced hyperglycaemia can develop.[4] However, spontaneous hypoglycaemia can occur as a result of critical illness.[5] Both stress-induced hyperglycaemia and spontaneous hypoglycaemia are seen in patients with and without diabetes, and they are associated with worse outcome, especially when spontaneous hypoglycaemia is present.[4 6] Blood glucose measurement is a simple, widely used biomarker recorded in the EMS, which makes it feasible to use as an additional parameter in NEWS.

We hypothesised that the addition of plasma glucose measurement to NEWS in the prehospital setting could better identify patients at risk of death at 24 hours and at 30 days than standard NEWS.

METHODS

Study design

We conducted a retrospective cohort study based on electronic EMS patient records. No ethics approval was needed as no direct patient contact was conducted. We studied if adding glucose as an

additional parameter in NEWS would better identify the risk of death than NEWS alone.

Participants

We included all patients aged 18 years or older encountered by EMS from 17 August 2008 to 19 December 2015 in the district of Helsinki and Uusimaa who had all NEWS parameters and a blood glucose value measured. Exclusion criteria consisted of age under 18 years, invalid personal identity number, missing or invalid NEWS data or plasma glucose not measured by EMS.

Setting

Helsinki University Hospital has the responsibility to organise and supervise EMS for about 1.6 million inhabitants in the Helsinki metropolitan area. The EMS consist of a three-tiered system with basic life support, advanced life support and two physician-staffed units. If the patient does not require further medical treatment, the patient may be left at the scene. They all use the same electronic patient record system (MerlotMedi, CGI Suomi Oy, Helsinki, Finland).

Vital parameters (systolic BP, respiratory rate, HR and blood oxygen saturation) were recorded by paramedics via a monitor–defibrillator or manually (respiration rate, level of consciousness on GCS and temperature) on scene in the electronic EMS database from which the study data were extracted. Each aspect of GCS was separately recorded into the EMS electronic data. The devices used during the study period included Zoll M series and X series (Zoll Medical Corporation Inc, Chelmsford, Massachusetts, USA) and LifePak 12 and 15 (Physio-Control Inc, Redmond, Washington, USA). Paramedics measured blood glucose values according to local protocol mainly from capillary samples using plasma calibrated analysing device (Optimum Xceed glucometer and MediSense Optimum electrodes, Abbott Laboratories, Alameda, California, USA). The local protocol indicated a need for glucose measurement in patients with lowered level of consciousness, sudden deterioration of overall wellness from an unknown cause, disorientation or aggressiveness, seizure, a diabetic patient who is feeling unwell or hypothermia.

NEWS was calculated retrospectively from the EMS database records. Initial respiration rate, systolic BP, temperature and GCS score were used. For parameters that were recorded continually (HR and blood oxygen saturation), the mean value during the first 5 min was used to eliminate effect of artefact values caused, for example, by movement of patient's arm.

Survival of the patients was determined using the Finnish Population Register Centre records, which has complete national mortality data due to Finnish legislation. Patients were identified using their personal identification number.

Patient and public involvement

No patient involved.

Data analysis

Each NEWS parameter may receive 0–3 points depending on derangement from normal values. NEWS is categorised as aggregate low (0–4), medium (aggregate 5–6 or 3 points from an individual parameter) and aggregate high (≥7).[7] For study purposes, we categorised mental status using AVPU (an acronym for alert, voice, pain and unresponsive), and this was calculated from GCS as presented by Smith *et al*: A (GCS 14–15), V and P (GCS ≤13) and U (GCS ≤8).[2] Hyperglycaemia was defined as 11.1 mmol/L or above according the stress-induced hyperglycaemia cut-off value, and hypoglycaemia was defined as 3.0 mmol/L or less according using the severe hypoglycaemia cut-off value defined in reference ranges of the Europe Medicine Agency and American Diabetes Association.[8–10] Moderate hypoglycaemia (3.1–3.8 mmol/L) and moderate hyperglycaemia (5.6–11.0 mmol/L) were categorised as normoglycaemia for study purpose. Mortality at 24 hours and 30 days were used as outcome measures.

Statistical methods

Continuous variables are presented as median and IQR. Categorical data are presented as percentages with 95% CIs. Continuous variables are compared by Mann-Whitney U test and categorical variables by χ^2 test. Multivariate logistic regression model was used to calculate ORs with 95% CIs for risk of death for individual NEWS parameter categories.

Parameter estimates from the regression models were used to weight parameter point values (1–3) for glucose. Based on the ORs of the glucose disturbances, points for glucose were: normoglycaemia: 0, hypoglycaemia: 3 and hyperglycaemia: 1. Non-parametric local regression plots were done using loess method to compare the estimated risks per score point against the observed risks at 24 hours and at 30 days. Two-tailed p values <0.05 were considered statistically significant.

Discrimination of the NEWS and NEWS with glucose (NEWSgluc) scores was evaluated by area under the receiver operational curve (AUROC) and by calculating sensitivities and specificities. Positive and negative likelihood ratios (LR+ and LR−) were calculated for NEWSgluc and NEWS cut-off points 1, 4, 7, 10 and 15. Regression models for NEWS score and NEWSgluc score were compared using likelihood ratio tests (LRTs). Model calibrations were plotted and tested using Hosmer-Lemeshow test.

We also assessed reclassification for the two models using continuous net reclassification index (cNRI). cNRI is used to describe the net proportion of subjects reclassified correctly by the NEWSgluc compared with NEWS alone. In general, cNRI is the sum of the proportion of event and non-event observations that were correctly reclassified by the new model.

Statistical testing was carried out using Graph Pad 7.0 MAC OS X. (Graph Pad Software, San Diego, California, USA) and R ((R Foundation for Statistical Computing. R Core Team: A language and Environment for Statistical Computing, 2018 (version 3.4.4)) using packages ggplot2 (Wickham H. ggplot2: Elegant Graphics for data analysis, 2016 and Anon. Annotation for 'ggplot2'. R package version 0.9.2.), cowplot (Wilke C. cowplot: Streamlined Plot Theme and Plot, 2017), plotROC, pROC and ResourceSelection (Lele SR, Keim JL. Resource Selection: Resource Selection (Probability) Functions for Use-Availability Data, R package version 0.3–2, 2017).

RESULTS

Demographics

A total of 750 694 ambulance calls occurred during the study period in this single EMS. Of those, 18% (95% CI 17% to 18%) lacked data. Blood glucose was measured in 49% (361 174) of all cases. All parameters to calculate NEWS and a blood glucose measurement were available in 4% (27 141) of cases (figure 1). Of those, data were unavailable for 0.2% (95% CI 0.2% to 0.3%). Median age of the studied population was 69 years and 48.1% were male (table 1). Of the included patients, 1.0% (95% CI 0.8% to 1.0%) had blood glucose level of 3.0 mmol/L or less and 13.4% (95% CI 13.0% to 13.8%) had blood glucose level of 11.1 mmol/L or above. Mortality was 0.7% (95% CI

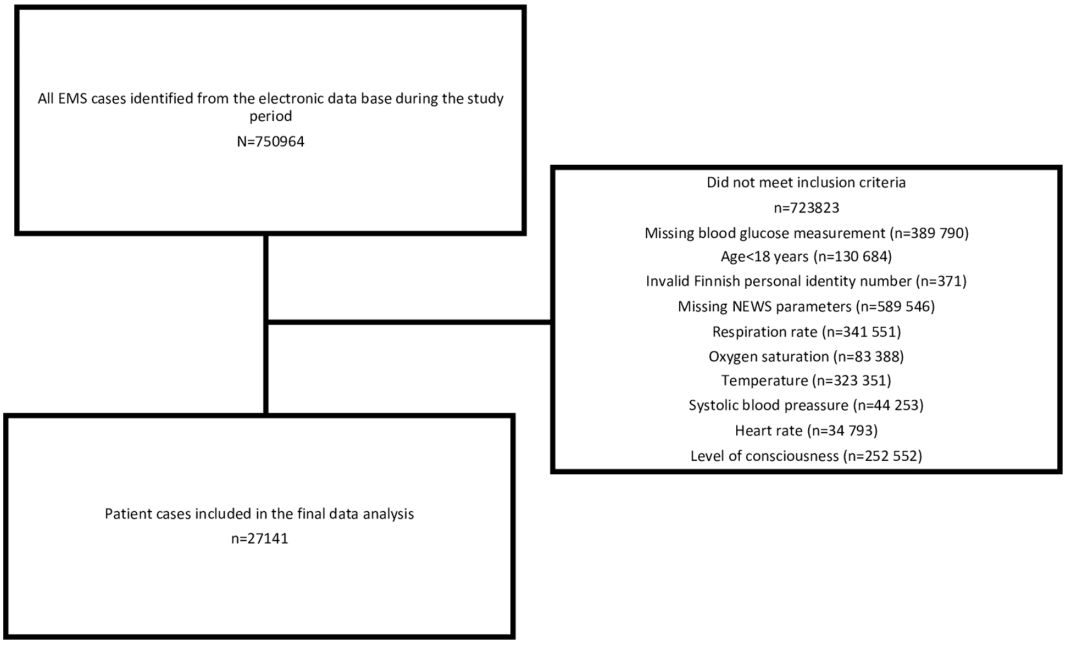

Figure 1 Inclusion and exclusion of study patients. EMS, emergency medical services; NEWS, National Early Warning Score.

0.6% to 0.9%) at 24 hours and 3.5% (95% CI 3.3% to 3.7%) at 30 days.

Outcome

Multivariable logistic regression model revealed that abnormal blood glucose, especially hypoglycaemic values, had ORs for identification of mortality risk comparable or higher than other variables of traditional NEWS parameters (table 2). Only categories, 'HR <40/min', 'breathing rate >25/min' and 'level of consciousness parameter'", identified more risk of death at 24 hours than hypoglycaemia. At 30 days, only 'blood oxygen saturation <91%' exceeded hypoglycaemia as an identification for risk of death.

Based on the ORs from multivariable regression model, NEWSgluc had the following scoring: normoglycaemia: 0, hypoglycaemia: 3 and hyperglycaemia: 1.

The AUROC showed similar discrimination for NEWS and NEWSgluc score for identification of risk of mortality at 24 hours. The NEWSgluc score achieved an AUROC of 0.851 (95% CI 0.827 to 0.875) compared with AUROC of 0.844

Table 1 Demographics and vital sign of patients included in the study and the whole population treated during the study period

	Study population	Study, population: severe hypoglycaemia (≤3.0 mmol/L)	Study population: severe hyperglycaemia (>11.1 mmol/L)	All EMS patients >18 years treated during the study period
N	27 141	250	3631	750 964
Age (year)	69 (52 to 81)	62 (50 to 75)	74 (62 to 83)	63 (44 to 79)
Sex, male (%)	48 (47 to 49)	62 (56 to 68)	47 (46 to 50)	–
Systolic BP (mm Hg)	142 (122 to 164)	136 (116 to 157)	142 (121 to 164)	140 (124 to 160)
Temperature (°C)	36.8 (36.3 to 37.3)	35.8 (34.6 to 36.5)	36.9 (36.4 to 37.5)	36.8 (36.4 to 37.3)
Blood oxygen saturation (%)	96 (93 to 98)	96 (92 to 98)	95 (91 to 97)	97 (95 to 98)
HR (/min)	87 (73 to 103)	86 (73 to 101)	92 (76 to 108)	87 (74 to 102)
Respiratory rate (/min)	16 (15 to 20)	16 (15 to 20)	18 (16 to 25)	16 (15 to 18)
GCS	15 (15 to 15)	15 (13 to 15)	15 (15 to 15)	15 (15 to 15)
Supplemental oxygen given (%)	15 (14 to 15)	16 (12 to 21)	25 (24 to 27)	6 (6 to 6)
First prehospital blood glucose (mmol/L)	7.3 (6.0 to 9.1)	1.9 (1.1 to 2.5)	13.6 (12.0 to 16.9)	–
Dispatch priority:				
A	7 (7 to 7)	19 (15 to 25)	8 (8 to 9)	5 (5 to 5)
B	38 (38 to 39)	45 (39 to 51)	37 (35 to 38)	20 (19 to 20)
C	48 (47 to 49)	31 (26 to 37)	49 (48 to 51)	36 (36 to 36)
D	6 (6 to 7)	4 (2 to 8)	8 (7 to 9)	22 (22 to 22)

Data are presented as medians and IQRs except for sex, supplemental oxygen given, dispatch codes and data unavailable, which are presented as percentages with 95% CIs. In column 'All patients', the proportion of patients with each variable varied.
A, B, C and D=dispatchpriorities.
A=highest priority.
D=lowest priority.
EMS, emergency medical services.

Table 2 ORs 95% CI for individual NEWS parameters as variables

		24 hours		30 days	
NEWS parameter	**Parameter levels**	**OR (95% CI)**	**P value**	**OR (95% CI)**	**P value**
Respiratory rate	12–20 times/min	1 (reference)		1 (reference)	
	≤8 times/min	3.30 (1.21 to 7.58)	0.010	1.75 (0.92 to 3.07)	0.067
	9–11 times/min	1.53 (0.44 to 4.02)	0.442	1.57 (0.85 to 2.7)	0.123
	21–24 times/min	2.12 (1.29 to 3.36)	0.002	1.62 (1.3 to 2.01)	<0.001
	≥25 breaths/min	3.88 (2.73 to 5.55)	<0.001	2.16 (1.82 to 2.55)	<0.001
Blood oxygen saturation	≥96%	1 (reference)		1 (reference)	
	≤91%	2.55 (1.75 to 3.74)	<0.001	2.99 (2.5 to 3.58)	<0.001
	92%–93%	1.29 (0.73 to 2.2)	0.360	1.97 (1.57 to 2.47)	<0.001
	94%–95%	1.01 (0.60 to 1.64)	0.970	1.32 (1.07 to 1.63)	0.010
Level of consciousness	A	1 (reference)		1 (reference)	
	V, P or U	4.12 (3.03 to 5.59)	<0.001	2.74 (2.35 to 3.19)	<0.001
HR	51–90 times/min	1 (reference)		1 (reference)	
	≤40 times/min	5.11 (1.13 to 16.42)	0.014	3.85 (1.5 to 8.54)	0.002
	41–50 times/min	1.45 (0.54 to 3.22)	0.410	1.79 (1.11 to 2.76)	0.011
	91–110 times/min	0.98 (0.68 to 1.39)	0.911	1.09 (0.93 to 1.28)	0.297
	111–130 times/min	0.96 (0.61 to 1.47)	0.846	1.00 (0.81 to 1.23)	0.983
	≥131 beats/min	0.87 (0.41 to 1.66)	0.702	1.02 (0.74 to 1.39)	0.881
Systolic BP	111–219 mm Hg	1 (reference)		1 (reference)	
	≤90 mm Hg	2.29 (1.48 to 3.44)	<0.001	1.75 (1.37 to 2.21)	<0.001
	91–100 mm Hg	1.60 (0.89 to 2.69)	0.094	1.59 (1.20 to 2.07)	<0.001
	101–110 mm Hg	0.90 (0.48 to 1.56)	0.726	1.13 (0.87 to 1.45)	0.337
	≥220 mm Hg	2.95 (1.2 to 6.18)	0.009	1.41 (0.8 to 2.31)	0.199
Temperature	36.1°C–38.0°C	1 (reference)		1 (reference)	
	≤35°C	2.98 (1.83 to 4.72)	<0.001	1.64 (1.23 to 2.16)	<0.001
	35.1°C–36.0°C	2.27 (1.57 to 3.25)	<0.001	1.33 (1.09 to 1.06)	0.003
	38.1°C–39.0°C	0.85 (0.45 to 1.50)	0.603	1.14 (0.89 to 1.44)	0.285
	≥39.1°C	1.10 (0.52 to 2.08)	0.780	0.80 (0.56 to 1.13)	0.226
Supplemental oxygen given	No	1 (reference)		1 (reference)	
	Yes	1.26 (0.91 to 1.75)	0.165	1.22 (1.03 to 1.44)	0.018
Glucose	Normal	1 (reference)		1 (reference)	
	Hyperglycaemia	1.57 (1.12 to 2.18)	0.008	1.45 (1.23 to 1.70)	<0.001
	Hypoglycaemia	3.69 (1.85 to 6.87)	<0.001	2.06 (1.28 to 3.19)	0.002

Level of consciousness: A=alert, V=responds to voice, P=responds to pain and U= unresponsive (according to the Royal College of Physicians).[7]
NEWS, National Early Warning Score.

(95% CI 0.818 to 0.869) with the standard NEWS score. Similar results were obtained with identification of risk of mortality at 30 days with an AUROC of 0.756 (95% CI 0.741 to 0.772) for NEWSgluc score and an AUROC of 0.753 (95% CI 0.737 to 0.768) for standard NEWS score.

Similar specificity and sensitivity results at cut-off points 1, 4, 7, 10 and 15 for NEWS and NEWSgluc score for 24hours and 30-day mortality are presented in table 3. However, at lower cut-off values, severe hypoglycaemia and severe hyperglycaemia are under-represented and hence sensitivities or specificities are not markedly changed between the two models. Positive and negative likelihood ratios of NEWS and NEWSgluc are similarly not markedly different with lower cut-off points, as they are dependent on given sensitivities and specificities. At cut-off point 15, which represents a more deranged body homeostasis, NEWSgluc has a higher positive likelihood ratio at 24 hours and at 30 days. This means that NEWSgluc can better discriminate non-survivors at higher NEWS score.

Comparing NEWS and NEWSgluc using LRTs, the addition of glucose improved the scores significantly at 24 hours and at 30 days (both $p<0.001$).

The loess regression plots show how the NEWS and NEWSgluc scores discriminate the 24-hour and 30-day mortality (figure 2). The scores perform similarly, but the increased range of the NEWSgluc also leads to an increased risk estimate range in both cases but especially at 24-hour mortality. Models calibrated well according to the Hosmer-Lemeshow test (all p values were not significant), and the addition of glucose improved the calibration of the identification of the 24-hour mortality risk (figure 3).

The events and non-events that were reclassified correctly for NEWSgluc at 24-hour and 30-day mortality risk are presented in table 4. The NEWSgluc correctly reclassified 6.4% into a higher risk category for 24-hour mortality and 4.2% for 30-dday mortality, respectively. Among survivors 2.6% of the patients were incorrectly classified to have a higher risk category than with the NEWS.

Assessment of reclassification showed overall improvement for accurately detecting outcomes using NEWSgluc compared with NEWS (table 5). Groupwise cNRI checks the reclassification in a specified category, here survivors and non-survivors, and cNRI is a sum of these comparisons from three groups (severely

Table 3 Sensitivities, specificities and LRs of NEWS and NEWSgluc scores

	24-hour mortality		30-day mortality	
	NEWS	NEWSgluc	NEWS	NEWSgluc
Cut-off				
1				
Sensitivity	0.99	0.99	0.95	0.96
Specificity	0.18	0.17	0.19	0.17
LR+	1.21	1.19	1.17	1.16
LR–	0.08	0.06	0.26	0.22
4				
Sensitivity	0.90	0.91	0.76	0.78
Specificity	0.61	0.59	0.62	0.60
LR+	2.29	2.22	2.00	1.96
LR-	0.17	0.15	0.38	0.36
7				
Sensitivity	0.71	0.75	0.51	0.54
Specifity	0.83	0.81	0.83	0.82
LR+	4.07	4.05	3.10	3.03
LR–	0.35	0.30	0.58	0.56
10				
Sensitivity	0.39	0.41	0.24	0.27
Specificity	0.94	0.93	0.94	0.94
LR+	6.59	6.00	4.44	4.44
LR–	0.65	0.63	0.80	0.80
15				
Sensitivity	0.04	0.08	0.02	0.03
Specificity	1.00	1.00	1.00	1.00
LR+	13.50	17.78	7.76	8.55
LR–	0.96	0.92	0.98	0.97

LRs, likelihood ratios; NEWS, National Early Warning Score; NEWSgluc, NEWS with glucose.

hyperglycaemic patient group, normoglycaemic patient group and severely hypoglycaemic patient group). Severely hyperglycaemic and severely hypoglycaemic patient groups received higher scores leading to an improvement in the cNRI for the non-survivors group when comparing NEWS and NEWSgluc score. Conversely, for the same reason cNRI in the survivors group decreased as the non-normoglycaemic patients received higher scores despite surviving. However, since the severely hyperglycaemic and severely hypoglycaemic patients were more

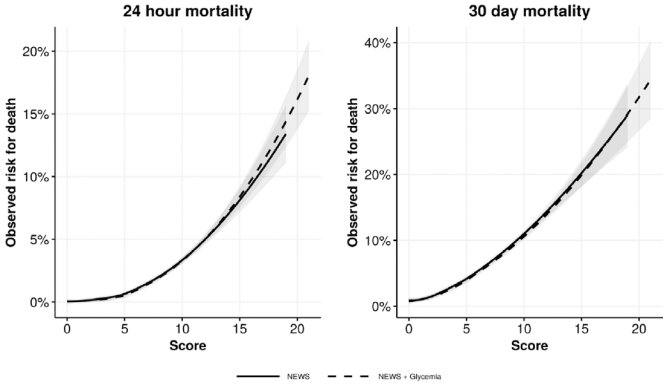

Figure 2 Loess regression plots for the NEWS against the observed risk for mortality. The shaded areas represent 95% CIs. NEWS, National Early Warning Score.

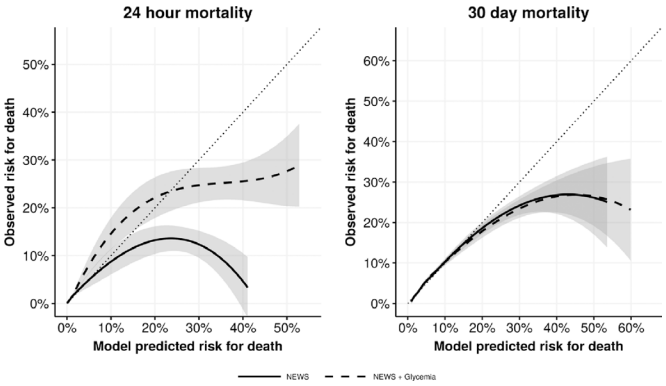

Figure 3 Calibration of models at 24 hours and at 30 days. The shaded areas represent 95% CI.

common in the non-survivors, the overall cNRI was improved by the addition of blood glucose to the NEWS.

DISCUSSION

In this retrospective study of over 27 000 patients transferred by EMS, we found that sensitivities, specificities and AUROC were similar between NEWS and NEWSgluc. However, likelihood ratios and reclassification test showed overall better identification with NEWSgluc of 24 hours risk of death compared with standard NEWS in the prehospital setting. Risk estimation for identification of mortality risk revealed glucose added value to NEWS aggregate points both at 24 hours and at 30 days, especially when severe hypoglycaemia was present. Addition of

Table 4 Events and non-events for NEWSgluc reclassification

24-hour mortality			
Events=202			
	NEWSgluc		
NEWS	Low	Medium	High
Low	26	4	1
Medium	0	20	8
High	0	0	143
Non-events=26 939			
	NEWSgluc		
NEWS	Low	Medium	High
Low	18 409	372	29
Medium	0	3152	296
High	0	0	4681
30-day mortality			
Events=943			
	NEWSgluc		
NEWS	Low	Medium	High
Low	278	17	1
Medium	0	141	22
High	0	0	484
Non-events=26 198			
	NEWSgluc		
NEWS	Low	Medium	High
Low	18 157	359	29
Medium	0	3031	282
High	0	0	4340

Low=0-4 points; medium=aggregate 5–6 points or 3 points from an individual parameter; and high=aggregate ≥7 points.

Table 5 Reclassification test results comparing the NEWS and NEWSgluc scores presented as percentages with 95% CI

Reclassification test	Risk of 24-hour mortality	P value	Risk of 30-day mortality	P value
cNRI	0.207 (0.141 to 0.273)	<0.001	0.127 (0.098 to 0.156)	<0.001
Groupwise cNRI (survivors)	−0.144 (−0.148 to −0.140)	<0.001	−0.141 (−0.145 to −0.137)	<0.001
Groupwise cNRI (non-survivors)	0.351 (0.286 to 0.417)	<0.001	0.268 (0.240 to 0.297)	<0.001

95% CI in brackets.
cNRI, continuous net reclassification index; NEWS, National Early Warning Score; NEWSgluc, NEWS with glucose.

glucose increased the score for 35% of the patients who died within 24 hours and for 27% of the patients who died within 30 days. Altogether, NEWSgluc better discriminated mortality of the patients when compared with the standard NEWS by taking the increased risk of mortality of severely hyperglycaemic and severely hypoglycaemic patients into account.

Stress induced hyperglycaemia, defined as plasma glucose 11.1 mmol/L or above during acute illness, is considered to be a physiological response with complex involvement of immune response, hypothalamic–pituitary axis, early insulin deficiency and later insulin resistance along with derangements of counter-regulatory hormones (adrenalin, glucagon, cortisol and growth hormone).[4] As moderate or highly elevated NEWS score is a sign of derangement in body physiology, a combination of elevated blood glucose level (≥11.1 mmol/L) together with an elevated NEWS score is likely to be stress induced. In the hypoglycaemic cases, especially with high NEWS, hypoglycaemia may be a sign of failure of counter-regulatory hormones to respond to physiological stress during critical illness, which is associated with high mortality.[11]

However, in previous studies adding blood glucose to a scoring system added modest or no benefit.[12–17] None of these studies were performed in a prehospital setting. Blood glucose was either without categorisation or only hyperglycaemia was considered in varying degrees: Cattermole *et al* (blood glucose ≥7.0 mmol/L), Timotéo *et al* (blood glucose ≥8.9 mmol/L), Glassberg *et al* (blood glucose ≤11.1 mmol/L and ≥11.1 mmol/L) and McCall *et al* with normoglycaemia, modest hyperglycaemia (7.9–11 mmol/L) and stress-induced hyperglycaemia (≥11.1 mmol/L), respectively.[12–14 16] Hence, aside from Glassberg *et al* and McCall *et al*, these previous studies used mainly normoglycaemic or modest hyperglycaemic values, which are not good markers of critical illness. This may explain why only modest or no benefit was observed in the previous studies, whereas we found a significant improvement of the model if glucose was included.

Of the previous studies, one relied on AUROC[12] and one on likelihood ratio.[13] Most study analyses used logistic regression analysis.[14–17] Only Timotéo *et al* and van Toorenburg *et al* also used reclassification.[14 15] Risk of mortality was used as an outcome measure in four studies.[12 14 16 17] Abbott *et al*[17] studied adding blood glucose to NEWS. All other studies used different scoring systems: Global Registry of Acute Coronary Events, Injury Severity Score, Prince of Wales Emergency Department Score and stroke subtype, Oxford community Stroke Project classification, age and prestroke modified Rankin.[12–16] These scoring systems differed so much from NEWS that any valid comparison could not be truly made.

The statistical approaches used in the current study produced a slightly conflicting result. AUROC is widely used as a discrimination model to evaluate diagnostic tests, but it is not without problems. One disadvantage is that AUROC is a binary model, where only predetermined thresholds are used for analysis depending on used sensitivity and specificity, thus lacking the goodness-of-fit modelling and individual cofounding factors.[18 19] AUROC is also an insensitive measurement when exploring variables to add to a prediction score or model.[20] Calibration of the models as well as risk reclassification can also reveal valuable information when comparing the models.[19 20] Using them in conjunction with AUROC leads to a more thorough insight of the performance of the new model. This was the case with the addition of blood glucose to NEWS. The AUROC did not differ between the models, but the models calibrated better, leading to improved reclassification. As NEWS is used to identify risk of death, calibration and risk classification are both important aspects of the model.

In the prehospital settings, risk stratification is even more challenging compared with hospital surroundings due to timely intervention of patient care and with constantly changing surroundings. Hence, when studying adding additional parameters to NEWS, we need to keep in mind that NEWS utilisation should altogether be optimised. The main pitfall is often lack of data gathering and human errors.[21] To help NEWS to better serve its purpose, implementation of automatic coupling of NEWS data, routine collection of NEWS data is needed, perhaps using automatic entry of these parameters into the electronic database recordings. With these changes, NEWS could even better help further study designs in the future.

The main limitations of the current study are, first, that only specified patients received a blood glucose measurement according to local protocol, and complete data were available only from 4% of all patients encountered by the EMS during the study period. Second, the study design was a retrospective design. The study carries a high risk of selection bias as only patients with all necessary data available were included. This may limit generalisation of these study results. From vital sign parameters, respiratory rate is known to be the least recorded parameter.[22] In our study temperature, respiratory rate and level of consciousness needed manual recording. In many cases, the patient is likely to have normal vital signs, for instance in psychiatric disorders or with minor complaints, the EMS personnel uses clinical assessment and often does not take any vital signs. Also, not all EMS cases have actual patient contact. These cases result in empty patient records regarding vital signs. More severe cases are more thoroughly assessed, and it is likely that they carry all vital parameters for NEWS calculation. As a result, it is possible that more severe cases are emphasised in our study population along with blood glucose disturbances and higher risk of death. Both models, NEWS and NEWSgluc, still underestimate the risk of death in higher risk groups. This has to be taken into consideration as well when interpreting the results.

Furthermore, blood glucose is most likely measured more often on patients with diabetes. Imbalanced diabetes causes chronic blood glucose disturbances, which may cause greater blood glucose variability. This patient group is also at higher risk of developing stress-induced blood glucose disturbances and risk of death due their underlying chronic condition.[23] We did not separate diabetics and non-diabetics in the study as we wanted

to study the usefulness of plasma glucose values as an additional parameter to NEWS in screening a mixed EMS population, so diabetes status was not on our focus in this study design.

Although nourished patients may present with hyperglycaemic blood glucose values, it is unlikely that these patients would score high on other NEWS values without any underlying disturbance in their condition. However, we could not consider patients' previous medical condition, which may have affected the results. Patients may have had chronic underlying diseases, such as chronic pulmonary obstructive disease and advanced congestive heart condition with lower blood oxygen saturation levels or baseline BP values. These may have given falsely high NEWS points.[24] This should always be kept in mind when interpreting the results of NEWS. Other limitations were not excluding patients with a 'do not attempt resuscitation' order. Most of the plasma glucose values were capillary samples, which may affect the accuracy of the results.[25]

Further studies should be done with a prospective study design to confirm the findings of the current study. A case–control study, where diabetics and non-diabetic are studied separately, would help to find out if these groups would have had differences.

CONCLUSION

Adding plasma glucose as an additional parameter to NEWS in prehospital setting may improve identification of risk of death. Especially severe hypoglycaemia seems to add value in identifying risk of short-term mortality.

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ORCID iD

Hanna Vihonen http://orcid.org/0000-0002-6060-408X

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