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Clinical paper

The optimal duration of continuous respiratory rate monitoring to predict in-hospital mortality within seven days of admission – A pilot study in a low resource setting

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Abstract

Background: Currently there are no established benefits from the continuous monitoring of vital signs, and the optimal time period for respiratory rate measurement is unknown.

Setting: Low resource Ugandan hospital,

Methods: Prospective observational study. Respiratory rates of acutely ill patients were continuously measured by a piezoelectric device for up to seven hours after admission to hospital.

Results: 22 (5.5%) out of 402 patients died within 7 days of hospital admission. The highest c-statistic of discrimination for 7-day mortality (0.737 SE 0.078) was obtained after four hours of continuously measured respiratory rates transformed into a weighted respiratory rate score (wRRS). After seven hours of measurement the c-statistic of the wRRS fell to 0.535 SE 0.078. 20% the patients who died within seven days did not have an elevated National Early Warning Score (NEWS) on admission but were identified by the 4-hour wRRS. None of the 88 patients whose average respiratory rate remained between 12 and 20 bpm throughout four hours of observation died within 7 days of admission. A simple predictive model that included the four-hour wRRS, Shock Index and altered mental status had a c-statistic for 7-day in-hospital mortality of 0.843 SE. 0.057.

Conclusion: Four hours of continuously measured respiratory rates was the observation period that best predicted 7-day in-hospital mortality. After four hours the discrimination of a weighted respiratory rate score deteriorated rapidly.

Keywords: Respiratory rate, Patient monitoring, Physiology, Acute medicine, Technology

Introduction

During the early assessment of patients it is important to be sure that deterioration is noticed before it is too late to provide time-critical life-saving treatment. The National Early Warning Score (NEWS) is widely used to identify patients who need immediate attention and a single measurement is an excellent predictor of imminent mortality. However, 9% of deaths within 24-hours occurred in patients who present with a low NEWS value, and many patients who die in hospital have a low NEWS on admission.[1]

Although vital sign monitoring is key for the prediction of clinical deterioration, little is known about the changes and trends of individual vital signs during an acute illness in hospital[2] or their effectiveness in predicting hospital outcomes. It has been suggested that intermittently measured vital sign changes within the first 4–5 h

Abbreviations: 95% CI, 95% confidence interval, bpm, beats or breaths per minute, NEWS, National Early Warning Score, SD, standard deviation, SE, standard error, wRRS, weighted respiratory rate score

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https://doi.org/10.1016/j.resplu.2024.100768
Received 28 July 2024; Received in revised form 25 August 2024; Accepted 31 August 2024

of admission may be of little prognostic value, and only reliably predict outcome after 12 to 24 h.[3]

Respiratory rate is a component of most early warning systems,[4] and considered by some to be the most important vital sign.[5] Despite this, it is often recorded inaccurately or not at all,[6–7] and there is no gold standard for its measurement. Although it is probable that respiratory rate is the first vital sign to become deranged when patients deteriorate,[8] this hypothesis has been difficult to prove as the accurate continuous measurement of respiratory rate has been technically difficult. However, recently several respiratory rate devices using different technical approaches have become available,[9] including a piezoelectric, non-invasive, wireless, body worn, motion-tolerant and continuous respiratory rate monitor device, which has comparable accuracy to the capnograph.[10]

The aim of this study was to determine the optimal observation time of continuously measured respiratory rate required to predict short term in-hospital mortality (arbitrarily defined as within seven days of admission) of patients admitted to a low-resource hospital in sub-Saharan Africa, and to compare continuous respiratory measurements with other easily available outcome predictors.

Methods

Setting

This prospective, observational pilot study was conducted in Kitovu Hospital from 18th May 2023 to 31st January 2024 and conforms with STROBE guideline.[11] Kitovu Hospital has 248 beds (which includes 50 medical and 35 surgical) and is located near Masaka, Uganda, 140 km from the capital city of Kampala. It is a private not-for-profit hospital, accredited by the Uganda Catholic Medical Bureau.

Participants and study process

Participants were a convenience sample of consenting, non-pregnant, acutely ill patients, aged 18 year of age or older, who were admitted to the hospital's medical ward. Pregnant patients were excluded because they are never admitted to the medical ward and are always managed in the obstetric unit, which is some distance away. All other patients are admitted through a common emergency and out-patient department, which is only a few feet from the medical ward. Therefore, there was no delay to entering the medical ward once the decision to admit had been made. Study participants were selected if they were considered sick enough to justify continuous monitoring for up to seven hours. The decision to limit the duration of observation to seven hours was a pragmatic one, taken to reduce the risk of loss or damage of the piezoelectric devices and to ensure enough devices were available for new patients.

The clinical status and vital signs on admission of every participant were entered at the bedside using tablet computers into a clinical database system, which also required variables previously identified to be associated with in-hospital mortality to be entered; these included the patient's mental alertness, gait stability, HIV status, mid-upper arm circumference,[12] and calculation of the Shock Index (i.e., heart rate divided by systolic blood pressure).[13] Respiratory rates were counted using the *RRate* app, which calculates the respiratory rate from the interval between taps on a smartphone screen.[14] The database system automatically calculated and stored the admission National Early Warning Score (NEWS)[15] and recorded patient's status at discharge. All data entries were automatically time and date stamped. Patients who were alert, attentive, calm, and coherent (i.e., normal mental status) provided written informed consent, all other patients were assessed as having altered mental status and written informed consent was provided by their next of kin.

The respiratory rate measuring piezoelectric device (*RespiraSense*™, PMD Solutions, Cork, Ireland) was applied as soon as possible after admission to the patient and continuously streamed date and time stamped respiratory rate data by wireless to a secure server. If the device did not have to be removed for clinical or operational reasons it remained on the patient up to 7 h after admission. The hospital's usual standard of care is to make all patients vital signs and calculated NEWS values available to all clinicians. The respiratory rates displayed every 15 min by the piezoelectric device were also made available. However, how to respond to these values was left to each clinician's clinical judgement. During subsequent analysis the respiratory rates for each hour of observation were averaged, yielding an average value for each hour of observation after admission.

Outcomes

The primary outcome was in-hospital mortality within seven days of admission. Secondary outcomes were overall in-hospital mortality, and in-hospital mortality at intervals between admission and seven days.

Statistic methods and data analysis

All calculations were performed using Epi-Info version 6.0 (Centre for Disease Control and Prevention, USA) and logistic regression analysis using Logistic software.[16] The c-statistic of discrimination for mortality at different times of after admission was determined by the method of Hanley and McNeil; values of the c-statistic range from 0 to 1, 0.5 indicates no discrimination and good discrimination is generally considered to be a value >0.8.[17] A normal distribution was assumed for all continuous variables,[18] which were compared by using analysis of variance. Categorical variables were compared using Chi squared analysis with Yates' continuity correction. Youden's J statistic (i.e., sensitivity + specificity – 1) was used to determine values with the highest association with seven day in-hospital mortality.[19] The p-value for statistical significance was 0.05.

To capture the mortality risk associated with low respiratory rates, the average respiratory rate for each hour of observation up to seven hours after admission were weighted according to the NEWS weightings for respiratory rates (i.e., rates >=12 and <=20 bpm scored 0 points; rates >=9 and <=11 bpm scored 1 point; rates >=21 and <=24 bpm scored 2 points; and rates <=8 or >=25 scored 3 points).[15] These points calculated for each individual hour of observation were then summed so that after one hour of observation the maximum of this weighted respiratory rate score (wRRS) was three points, rising to a maximum of 21 points after seven hours.

Ethics

RespiraSense™ device is not sold in Uganda, and it required ethical approval to use. Ethical approval for the study was obtained from the Kampala International University (KIU-2021–45) and the Uganda

National Council for Science and Technology (UNCST HS2792ES). The study conforms to the principles outlined in the Declaration of Helsinki.

Results

A convenience sample of 402 patients participated in the study; their length of hospital stay was 3.3 SD 3.4 days (median 2.0, IQR 1,5 days), their mean age was 55.9 SD 22.9 (IQR 37,74) years, and 155 (38.6%) of them were men. On admission 161 (40.0%) patients needed help to walk or were bedbound (i.e., had an unstable gait), 64 (15.9%) had altered mental status, and 161 (40.0%) had a NEWS≥5. Thirty-four patients (8.5%) died while in hospital, 22 within a week of admission, and 10 during the second week after admission. Only heart rate, respiratory rate, shock index, NEWS, an unstable gait, and alerted mental status were significantly associated with death within a week of admission (Table 1).

All 402 patients had their respiratory rate continuously measured for at least one hour, 399 (99.3%) for two hours, 390 (97.0%) for three hours, 377 (93.8%) for four hours, 362 (90.0%) for five hours, 352 (87.6%) for six hours and 334 (83.1%) for seven hours. The c-statistic for the discrimination of 7-day in-hospital mortality of NEWS recorded on admission was 0.779 SE 0.64. This was compared to the c-statistic for the wRRS calculated from first to seventh hour of observation, which reached its highest value after 4 h of observation (0.737 SE 0.078); thereafter it rapidly declined (Fig. 1), so that after seven hours of observation it was only 0.535 SE 0.078 with only slightly more discrimination than a coin toss (Table 2). The highest c-statistic of the 4-hour wRRS was for death within 24 h (0.891 SE 0.214), and the lowest was 0.620 SE 0.059 for in-hospital death.

After one hour of observation 147 (39.0%) patients had an average respiratory rate between 12 and 20 bpm (i.e., one-hour wRRS zero points), and 2 (1.4%) subsequently died within 7 days. In contrast, none of the 88 patients with zero four-hour wRRS points (i.e., their average respiratory rate remained between 12 and 20 bpm throughout four hours of observation) died within 7 days, compared 10 of the 83 patients (12.0%) with 12 four-hour wRRS points (i.e., those whose average respiratory rates were persistently under 9 or over 24 bpm). The 206 remaining patients, with four-hour wRRS points ranging from 1 to 11, had a seven-day mortality rate of 4.4%; of the nine patients who died within seven days, seven had ≥2 wRRS points throughout their entire four hours of observation

The four-hour wRRS value with the highest Youden J statistic was >9 points, which had an odds ratio for seven-day in-hospital mortality of 5.62 (95%CI 1.82 – 18.53, p 0.0008). The Shock Index with the highest Youden J statistic for seven-day in-hospital mortality was 1.2 (odds ratio 7.80, 95% CI 2.33 – 25.48, p <0.0001). Of the 377 patients observed for four hours, 63 (16.7%) had a NEWS<5 and a 4-hour wRRS>9 points; 4 (6.3%) of these patients were among the 19 who died within seven days (Fig. 2). Only one of 163 patients with a NEWS<5 and 4-hour wRRS≤9 died within seven days; she was 69 years old, had altered mental status and an admission NEWS of 4.

Logistic regression analysis of altered mental status, unstable gait, NEWS >=5, a Shock Index > 1.2 and four-hour wRRS>9 points, found only altered mental status, shock index and wRRS remained significantly associated with seven-day in-hospital mortality (Table 3). A simple score that awarded one point for altered mental status, one for a shock index > 1.2, and one for a wRRS>9 points had a c-statistic for seven-day in-hospital mortality of 0.843 SE 0.057

Table 1 – Continuous and categorical variables of the study population. NEWS=National early warning score; SD=standard deviation; bpm = breaths or beats per minute.

	Continuous variables			
Variable	**Total**	**Alive**	**Died within 7 days of admission**	***P***
Number of patients	402	380	22	
Age (years)	55.9 SD 22.9	55.7 SD 23.0	59.5 SD 21.0	0.44
Length of stay (days)	3.3 SD 3.4	3.4 SD 3.5	1.9 SD 1.5	0.04
Heart rate (bpm)	87.9 SD 20.3	82.3 SD 18.9	98.6 SD 32.9	0.01
Systolic blood pressure (mmHg)	118.1 SD 24.8	118.2 SD 24.5	121.0 SD 33.3	0.61
Diastolic blood pressure (mmHg)	74.4 SD 16.9	74.4 SD 16.5	74.5 SD 23.9	0.97
Temperature (°C)	36.2 SD 0.5	36.2 SD 0.4	36.1 SD 0.6	0.61
Oxygen saturation (%)	96.5 SD 6.2	96.5 SD 6.2	96.1 SD 4.5	0.74
Manual respiratory rate (bpm)	22.0 SD 5.3	21.8 SD 5.1	24.2 SD 5.5	0.03
1st hour average respiratory rate by device (bpm)	22.6 SD 5.9	22.2 SD 5.5	28.1 SD 9.2	<0.0001
Shock index	0.78 SD 0.27	0.78 SD 0.25	0.91 SD 0.45	0.02
NEWS (points)	4.3 SD 3.0	4.1 SD 2.8	7.9 SD 4.0	<0.0001
Mid upper arm circumference (cm)	27.0 SD 4.0	26.9 SD 4.0	27.4 SD 2.9	0.57
	Categorical variables			
	No patients	**Odds ratio 7-day mortality**		***P***
Male sex	155 (38.6%)	1.35 (95%CI 0.52–3.45		0.65
HIV positive	36 (9.5%)	1.61 (95%CI 0.35–6.23		0.72
Diabetic	58 (15.4%)	0.91 (95%CI 0.21–3.45)		0.87
Unstable gait	161 (40.0%)	5.57 (95%CI 1.86–17.84)		0.0006
Altered mental status	64 (15.9%)	11.55 (95%CI 4.23–32.23)		<0.0001
NEWS >=5	161 (40.0%)	4.32 (95%CI 1.53–12.79)		0.003
Mid upper arm circumference < 20 cm	19 (4.7%)	0.96 (95%CI 0.00–7.48)		0.63

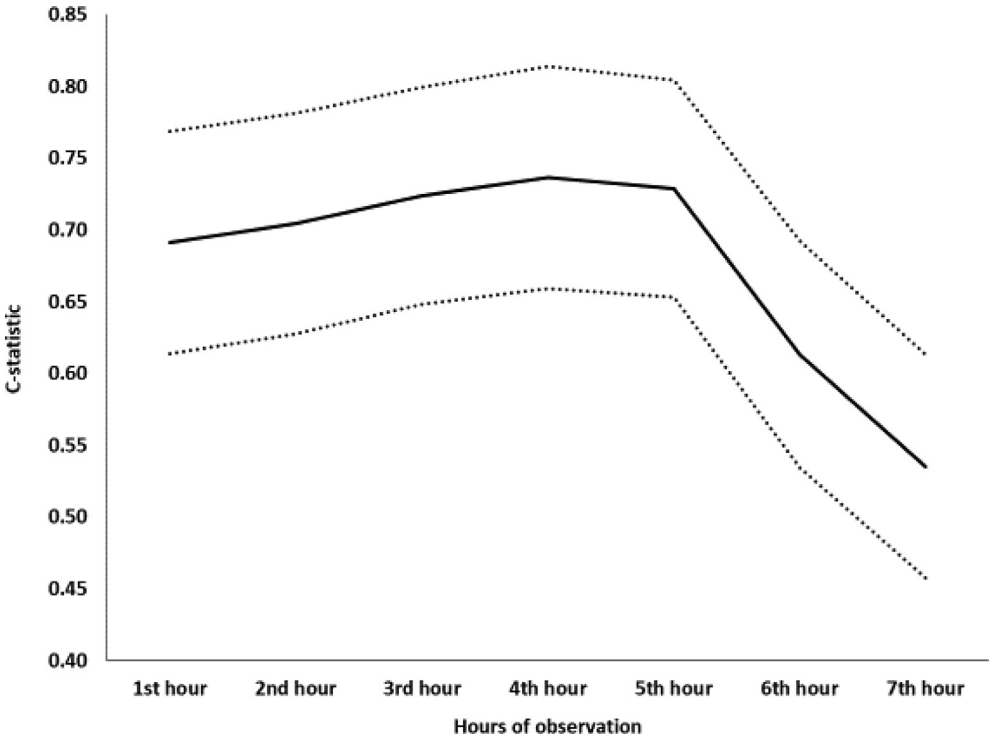

Fig. 1 – C-statistic of discrimination for death with 7 days of hospital admission of weighted respiratory rate scores (wRRS) according to hours of observation after admission. Solid line = C-statistic; dotted lines = standard error.

Table 2 – C-statistic for death in hospital within a week of admission of weighted Respiratory Rate Score (wRRS) from first to seventh hour of observation. Each row shows the c-statistic and its standard error (SE) at each hour of observation for the population that results were available for. Not all patients had their respiratory rate measured for seven hours i.e., only 344 patients (top row) had their respiratory measured continuously for seven hours, compared with the entire study population of 402 patients (bottom row) who had their respiratory rate measured continuously for one hour.

			C-statistic for death in hospital within a week of admission of weighted Respiratory Rate Score (wRRS) from first to seventh hour of observation						
Hours observed			1st hour	2nd hour	3rd hour	4th hour	5th hour	6th hour	7th hour
(Maximum points)			*(3)*	*(6)*	*(9)*	*(12)*	*(15)*	*(18)*	*(21)*
Number of patients									
Alive	Dead	Total							
319	15	334	0.691 SE 0.077	0.705 SE 0.077	0.724 SE 0.076	0.737 SE 0.078	0.729 SE 0.076	0.613 SE 0.079	0.535 SE 0.078
336	16	352	0.702 SE 0.075	0.716 SE 0.074	0.735 SE 0.073	0.746 SE 0.072	0.739 SE 0.073	0.620 SE 0.076	
345	17	362	0.712 SE 0.072	0.726 SE 0.071	0.744 SE 0.070	0.756 SE 0.069	0.751 SE 0.070		
358	19	377	0.694 SE 0.069	0.706 SE 0.068	0.714 SE 0.068	0.723 SE 0.068			
370	20	390	0.676 SE 0.068	0.685 SE 0.067	0.690 SE 0.067				
378	21	399	0.684 SE 0.066	0.696 SE 0.065					
380	22	402	0.661 SE 0.065						

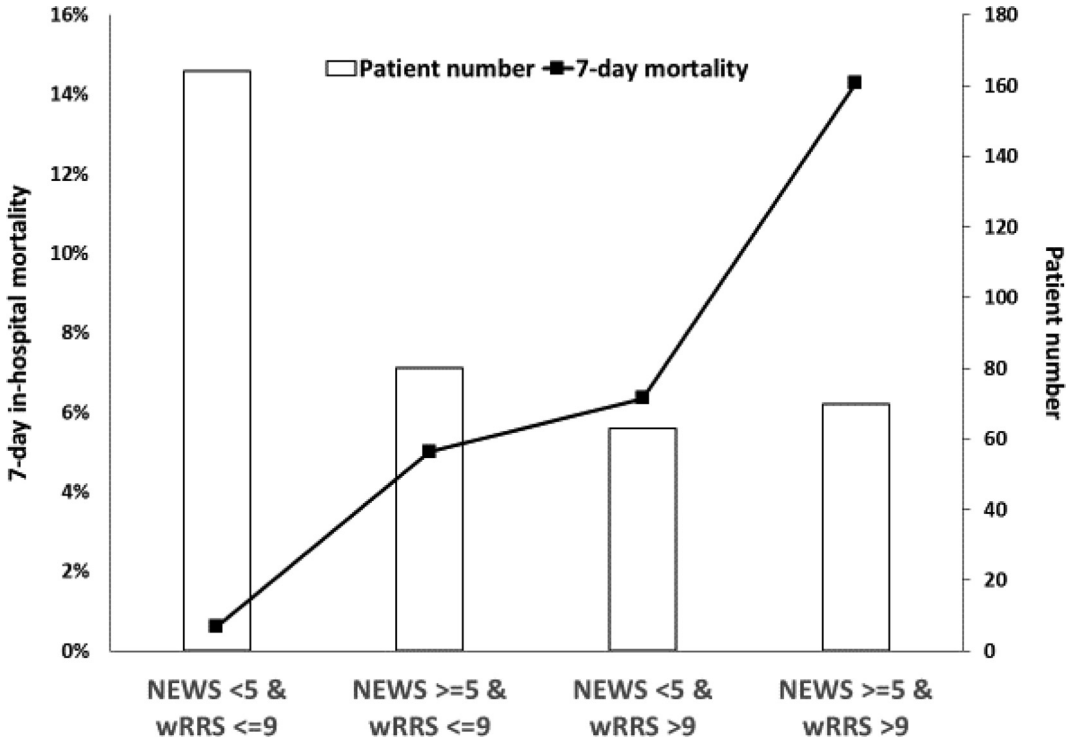

Fig. 2 – Seven-day in-hospital mortality of patients according to their admission National Early Warning Score (NEWS) and their four-hour weighted Respiratory Rate Score (wRRS).

Table 3 – Logistic regression model comparing 5 predictors for 7-day mortality. wRRS=weighted respiratory rate score. 95% CI=95% confidence interval. NEWS=National early warning score.

Variable	Coefficient (Standard error)		Odds ratio (95% CI)		*p*
Constant	−4.5236	(0.5912)			
NEWS >=5	0.0304	(0.6791)	1.03	(0.27–3.90)	0.96
Unstable gait	−0.2793	(0.8072)	0.76	(0.16–3.68)	0.73
Altered mental status	2.4399	(0.7714)	11.47	(2.53–52.04)	0.0016
Shock index > 1.2	1.5689	(0.7029)	4.8	(1.21–19.04)	0.026
wRRS>9	1.2405	(0.5846)	3.46	(1.10–10.87)	0.034

(Fig. 3). Only one of the 207 patients with zero points in this score died; he was 54 years old, HIV positive and had an admission NEWS of 5.

Discussion

Main findings

This pilot study found that when transformed into a weighted respiratory rate score (wRRS), the best observation period to predict 7-day in-hospital mortality from continuously measured respiratory rates immediately after admission was four hours. After four hours the discrimination of the wRRS deteriorates rapidly.

Interpretation

Patients with a poor prognosis and multiple comorbid conditions are more likely to be too sick to discharge and may, therefore, remain in hospital for a longer time. We postulated that deaths that occur early during hospitalization are more likely to be preventable and, therefore, selected death within 7 days as the study's primary outcome.

Respiratory rate fluctuates as it is under both voluntary and autonomic control, so that its measurement over time may be interrupted by speaking, swallowing and coughing. Moreover, it may be transiently increased by anxiety, movement and other exertions such as micturition and defecation (see Supplemental figure). Although it is quantified in breaths per minute (bpm), it is unlikely that a a single measurement captured over a few seconds is the best measurement period Our decision to average respiratory rates over one hour was an arbitrary one, and it may not be the optimal. Drummond[20] has shown that acutely ill medical patients often have abnormal breathing patterns and has argued that these variations over time may explain the frequently observed discrepancies between respiratory rate measurements.[21]

We found placing respiratory rates into range categories was an important insight, and future research may improve on the NEWS ranges we used. NEWS was devised so that zero points were

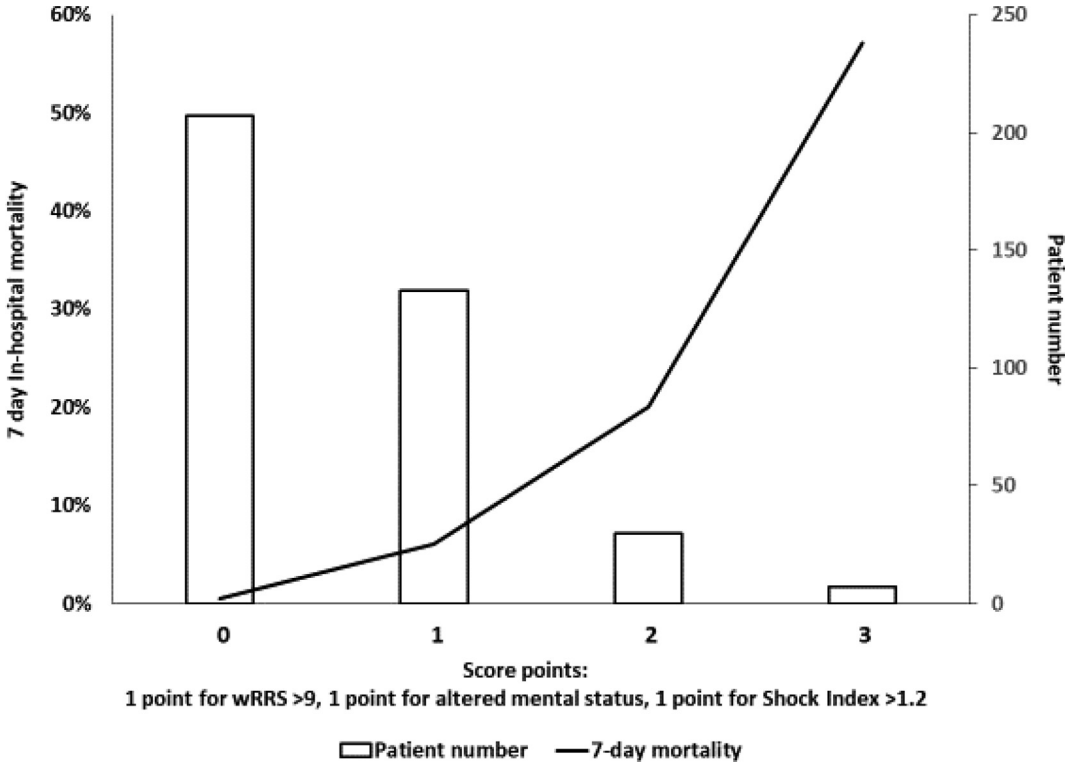

Fig. 3 – Seven-day in-hospital mortality according to a simple score that awarded one point for altered mental status, one for a shock index >1.2, and one for a four-hour weighted Respiratory Rate Score (wRRS) >9 points.

awarded to the range of respiratory rates associated with the lowest risk of death, and that variation within this range might be assumed to be normal physiologic fluctuations.[22] Our results confirmed this, as no patients who maintained average rates for four hours within this zero-point range (i.e., respiratory rates between 12 and 20 bpm) died within seven days of admission. However, it is possible that the true mortality could be as high as 3%.[23]

A possible explanation of our findings is patient fatigue, as severely ill patients may be unable to sustain the work of breathing. Two of our patients with zero wRRS points subsequently died in hospital, one after surgery for intestinal obstruction, and the other was an 88-year-old lady with chronic lung disease who died two weeks after admission from respiratory failure. It is possible that her 'normal' respiratory rate on admission was because she had already reached the terminal phase of her illness and was no longer able to maintain a higher rate of breathing. The work of breathing is considerable and usually accounts for about 5% of the total body oxygen consumption, which may rise to 30% in critically ill patients.[24] Therefore, a fall in the respiratory rate of a severely ill patients may not indicate improvement, but be a sign of serious deterioration and imminent death from impending respiratory failure.

Clinical significance

Although the benefits of continuous monitoring of vital signs by wearable devices have yet to be established,[25,26] our findings suggest that a four-hour period of respiratory rate monitoring may help improve emergency departments to risk stratify patients and make safer discharge decisions.[27] It is possible that frequent manual spot measurements over 4 h may give similar results. Many patients who die in hospital have a low NEWS on admission.[1] Although monitoring respiratory rate over 4 h had a c-statistic for 7-day mortality slightly less than NEWS measured on admission, 20% of the patients who died within seven days did not have an elevated NEWS on admission but were identified by four hours of respiratory rate monitoring.

Limitations

The small number of patients and outcomes, and lack of a validation cohort are the major flaws of this pilot study. Also, we do not know for how long patients were severely sick before they presented to hospital, and we do not know how many patients died shortly after discharge. The patients enrolled in the study did not present consecutively, but were a convenience sample of very sick patients, many of whom would have been in intensive care in better resourced settings. Therefore, our results may not be applicable to acutely ill patients attending emergency departments or admitted to acute medical wards elsewhere. For example, only 30% of patients admitted to UK hospitals have a NEWS >=3,[28] compared to 70% of our patients. We have previously reported that patients with a normal gait and a NEWS<3 on hospital admission had an in-hospital mortality <0.4% in Kitovu Hospital and two high-resource European hospitals. However, as we found in this study, immobile patients with a NEWS$\geq$3 had an in-hospital mortality of 14%, which was much higher than similar patients in the two European hospitals.[29]

The size of this single site study was limited by the resources available and was not large enough to allow what appear to be clinically important differences to reach statistical significance. Only 83% of our patients were continuously monitored for seven hours; reasons for discontinuing monitoring were numerous and included

removal by confused patients, anxious relatives, unauthorized or uninformed personnel, attempted theft, power cuts, and other misadventures.

We used the original version of NEWS as it remains comparable to the new NEWS2 version,[30] requires less data, is easier to calculate, and is, therefore, more appropriate to a low resource setting. Although we used the most widely reported NEWS cut-off of $\geq$5 points, similar results were obtained with second commonest cut-off values of $\geq$3 points.[1]

Conclusion

This pilot study shows that the use of continuously measured respiratory rate as a predictor for mortality and risk stratification may be more complex than anticipated and may require analysis of unknown variations, which may not be applicable to all patients, or all clinical settings. In this study of acutely ill patients just after admission to hospital, we found four hours of continuously measured respiratory rates, transformed into a weighted score, was the best observation period for the prediction of seven-day in-hospital mortality. After four hours the discrimination of the weighted respiratory rate score deteriorated rapidly. The risk stratification performance of the four-hour weighted respiratory rate score was enhanced by the addition of mental status assessment and measurement of the Shock Index.

Funding and conflict of interest statement

PMD Solutions supplied their *RespiraSense*^{TM} devices free of charge, all other costs were borne by the authors. Dr Rezvan Pakdel is an employee of PMD. None of the other authors have any potential conflicts of interest.

Role of the sponsors / Other contributions

PMD supplied the piezoelectric devices and extracted the respiratory rates recorded by them. RD (an employee of PMD) assisted the data analysis. PMD played no part in the conceptualisation or design of the study, or in drafting the paper.

Ethics declaration

Ethical approval for the study was obtained from the Kampala International University (KIU-2021-45) and the Uganda National Council for Science and Technology (UNCST HS2792ES). The study conforms to the principles outlined in the Declaration of Helsinki.

Authors contribution

FS and JK conceptualisation, data analysis and drafting of the paper, IN and JN collected data, RP data analysis, SN and AL administered the study and supervised data collection. All authors reviewed the final manuscript and corrected any errors.

Prior publication

There has been no prior publication in any form of this paper or the information it contains.

Data availability statement

Anonymized data of this study are available to all interested parties upon request.

CRediT authorship contribution statement

Franck Sikakulya: Data curation, Conceptualization. **Immaculate Nakitende:** Data curation. **Joan Nabiryo:** Data curation. **Rezvan Pakdel:** Formal analysis. **Sylivia Namuleme:** Project administration. **Alfred Lumala:** Project administration. **John Kellett:** Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

The authors wish to acknowledge Mr Pedro Asensio of PMD Solutions for his technical help.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.resplu.2024.100768.

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