

Single Deranged Physiologic Parameters Are Associated With Mortality in a Low-Income Country

Tim Baker, MBChB^{1,2,3}; Jonas Blixt, MD^{1,2}; Edwin Lugazia, MD, MMed⁴; Carl Otto Schell, MD^{5,6}; Moses Mulungu, MD, MMed⁷; Anna Milton, MD^{1,2}; Markus Castegren, MD, PhD⁵; Jaran Eriksen, MD, PhD⁸; David Konrad, MD, PHD^{1,2}

¹Department of Anaesthesia, Intensive Care and Surgical Services, Karolinska University Hospital, Stockholm, Sweden.

²Division of Anaesthesiology and Intensive Care Medicine, Department of Physiology and Pharmacology, Karolinska Institutet, Stockholm, Sweden.

³Global Health—Health Systems and Policy, Department of Public Health Sciences, Karolinska Institutet, Stockholm, Sweden.

⁴Department of Anaesthesia and Intensive Care, Muhimbili University of Health and Allied Sciences, Dar es Salaam, Tanzania.

⁵Centre for Clinical Research Sörmland, Uppsala University, Uppsala, Sweden.

⁶Department of Internal Medicine, Nyköping Hospital, Sörmland County Council, Nyköping, Sweden.

⁷Department of Anaesthesia and Intensive Care, Muhimbili National Hospital, Dar es Salaam, Tanzania.

⁸Division of Clinical Pharmacology, Department of Laboratory Medicine, Karolinska Institutet at Karolinska University Hospital Huddinge, Stockholm, Sweden.

Dr. Baker contributed to the conception and design of the study; acquired, analyzed, and interpreted the data; and drafted and revised the article. Dr. Blixt contributed to the conception and design of the study and acquired and interpreted the data. Dr. Lugazia contributed to the design of the study and acquired the data. Dr. Schell contributed to the conception and design of the study and interpreted the data. Dr. Mulungu contributed to the acquisition of data. Dr. Milton contributed to the conception and design of the study and acquired the data. Dr. Castegren contributed to data interpretation. Dr. Eriksen contributed to the design of the study and interpreted the data. Dr. Konrad contributed to the conception and design of the study and interpreted the data. All authors critically revised the article and approved the final article.

Dr. Baker received support for travel from the Association of Anaesthetists of Great Britain and Ireland and from the Karolinska Institutet Travel Grant (the funding sources had no role in the design, conduct, or reporting of the study). He is employed by Karolinska University Hospital and lectured for Karolinska Institutet. Dr. Baker and his institution received grant support from Olof Norlander Stipend and the Laerdal Foundation (the funding sources had no role in the design, conduct, or reporting of the study). Dr. Blixt is employed by Karolinska University Hospital. His institution received grant support from Karolinska Institutet, Stockholm, Sweden (travel grant for the study). Dr. Lugazia is employed by Muhimbili University of Health and Allied Sciences. Dr. Schell is employed by Landstinget Sörmland Medicinkliniken Nyköping Hospital. Dr. Mulungu is employed by Muhimbili National Hospital. Dr. Milton is employed by Karolinska University Hospital. Dr. Castegren is employed by Uppsala University/Karolinska University Hospital. Dr. Eriksen consulted for World Health Organization and is employed by Karolinska University Hospital. Dr. Konrad is employed by Karolinska University Hospital.

Address requests for reprints to: Tim Baker, MBChB, Department of Anaesthesia, Intensive Care and Surgical Services, Karolinska University Hospital, 171 76 Stockholm, Sweden. E-mail: timothy.baker@karolinska.se

Copyright © 2015 by the Society of Critical Care Medicine and Wolters Kluwer Health, Inc. All Rights Reserved.

DOI: 10.1097/CCM.0000000000001194

Objective: To investigate whether deranged physiologic parameters at admission to an ICU in Tanzania are associated with in-hospital mortality and compare single deranged physiologic parameters to a more complex scoring system.

Design: Prospective, observational cohort study of patient notes and admission records. Data were collected on vital signs at admission to the ICU, patient characteristics, and outcomes. Cut-offs for deranged physiologic parameters were defined a priori and their association with in-hospital mortality was analyzed using multivariable logistic regression.

Setting: ICU at Muhimbili National Hospital, Dar es Salaam, Tanzania.

Patients: All adults admitted to the ICU in a 15-month period.

Measurements and Main Results: Two hundred sixty-nine patients were included: 54% female, median age 35 years. In-hospital mortality was 50%. At admission, 69% of patients had one or more deranged physiologic parameter. Sixty-four percent of the patients with a deranged physiologic parameter died in hospital compared with 18% without ($p < 0.001$). The presence of a deranged physiologic parameter was associated with mortality (adjusted odds ratio, 4.64; 95% CI, 1.95–11.09). Mortality increased with increasing number of deranged physiologic parameters (odds ratio per deranged physiologic parameter, 2.24 [1.53–3.26]). Every individual deranged physiologic parameter was associated with mortality with unadjusted odds ratios between 1.92 and 16.16. A National Early Warning Score of greater than or equal to 7 had an association with mortality (odds ratio, 2.51 [1.23–5.14]).

Conclusion: Single deranged physiologic parameters at admission are associated with mortality in a critically ill population in a low-income country. As a measure of illness severity, single deranged physiologic parameters are as useful as a compound scoring system in this setting and could be termed “danger signs.” Danger signs may be suitable for the basis of routines to identify and treat critically ill patients. (*Crit Care Med* 2015; 43:2171–2179)

Key Words: critical care; developing countries; global health; hospital mortality; quality of health care; vital signs

Although critical care is a limited resource all over the world, this is especially the case in low-income countries (1, 2). Globally, the majority of critically ill patients are cared for in hospitals that lack advanced monitoring and medical equipment (3, 4). The sparse data that have been published about critical illness in low-income countries report high mortality rates of 27–43% (5–8).

Tanzania, a low-income country in East Africa, has a population of 47 million, and an annual health expenditure of \$38 per capita (9). Very few hospitals in Tanzania have ICUs, and there are structural barriers for critical care with deficiencies in infrastructure, human resources, training, and clinical routines (10).

The mainstay of critical care is monitoring and treating deranged physiology. Vital signs (heart rate, blood pressure, respiratory rate, conscious level, oxygen saturation, and body temperature) are markers of deranged physiology (11). Much recent work has focused on Early Warning Scores (12), rapid response teams (13), and goal-directed therapies (14, 15) that use vital signs to identify critical illness and trigger medical interventions. To define the trigger, these initiatives either use scoring systems that combine vital signs or use a defined level of abnormality of single vital signs. The single parameter abnormalities are markers of severely deranged physiology: once identified, an emergency response may be lifesaving. The initiatives have been developed in high-income countries and their utility has not been investigated in low-income country settings. We aimed to investigate whether single deranged physiologic parameters at admission to the ICU are associated with in-hospital mortality in Tanzania and compare single deranged physiologic parameters to a more complex scoring system.

MATERIALS AND METHODS

We conducted a prospective, observational cohort study of patient notes and admission records in the ICU at Muhimbili National Hospital (MNH) in Tanzania's largest city, Dar es Salaam.

Setting

MNH is a national referral hospital with 1,500 beds, receiving patients from the Dar es Salaam area (approximately 4 million inhabitants) and from other hospitals nationwide. The ICU is a closed six-bedded unit situated centrally in the hospital and is intended for all categories of patients with failing vital functions. During the period of the study, MNH had four specialists in anesthesia and intensive care who were responsible for care in the ICU, admitting patients and conducting ward rounds. They also had further duties in the 16 operating theaters and other acute care areas. The ICU nurses worked three 8-hour shifts with four to six nurses per shift. None of the nurses had formal intensive care qualifications. The ICU had six ventilators, suction machines, piped oxygen, and monitoring of electrocardiography, noninvasive blood pressure, and pulse oximetry. IV crystalloids, antibiotics, blood transfusions, adrenaline, and dopamine were available. Noradrenaline, other inotropes, and continuous sedation were not used. MNH was chosen as the site for the study due to the existence of an

ongoing international collaboration. The Muhimbili-Karolinska Anaesthesia and Intensive Care Collaboration was started in 2008 with the aim of improving anesthesia and intensive care through training, staff exchanges, guidelines, and research.

Study Population

The study population was all patients who were admitted and had completed their care in the ICU in a 15-month period between the study dates of November 11, 2012, and March 10, 2014. Patients lacking data on hospital outcome were excluded from the study and those lacking all vital sign observations at admission were excluded from all analyses except for the overall cohort size and outcome. Patients younger than 16 years old were excluded for all vital signs analyses as children do not have the same reference ranges as adults.

Deranged Physiologic Parameters

We used the cutoffs for deranged physiologic parameters in the Karolinska University Hospital's Medical Emergency Team protocol (16). The Karolinska protocol was chosen as it is simple and designed for wards without advanced monitoring facilities and is based on validated criteria (16, 17), and the Medical Emergency Team at Karolinska reduced in-hospital mortality by 10% (18). Two modifications were made to the Karolinska protocol. Glasgow Coma Scale (GCS) was modified to provide a static rather than dynamic cutoff as we were collecting data on only one occasion per patient, and we added a parameter for inspired oxygen as we hypothesized that high concentrations of oxygen therapy are a proxy for severe illness. Our parameters can be seen in **Figure 1**. For comparison, we used the National Early Warning Score (NEWS), the vital signs compound scoring system which has previously been shown to have the greatest ability

Conscious Level (Glasgow Coma Scale)	3-8
Respiratory Rate / minute	<8 or >30
Inspired Oxygen	80-100% or >10L/min
Oxygen Saturation (%)	<90
Heart Rate / minute	<40 or >130
Systolic Blood Pressure (mmHg)	<90

Figure 1. Deranged physiologic parameters used in the study.

to discriminate at-risk patients (12). As per NEWS standards, a score greater than or equal to 7 was defined as critical (19).

Data Acquisition

Preexisting routines at MNH included systematic hourly documentation of the patient's vital signs and treatments given on ICU observation charts. Four of the ICU nurses were given brief training as research assistants prior to the study and received a camera and computer. They photographed the ICU observation charts every day and uploaded the photographs to an encrypted, secure storage server. Data on vital signs at admission to the ICU were extracted from the photographs and entered into a database. If an observation chart was missing, admission vital signs were found in the patient's medical notes. Data on patient characteristics, dates of arrival and discharge, diagnosis, and ICU outcome were added from the charts and ICU admission books. Follow-up of the patients continued on the wards until hospital discharge or death. The primary endpoint for the study was in-hospital mortality. Post discharge follow-up was not possible in this setting.

Statistical Analysis

Stata (Release 12, StataCorp, College Station, TX) was used for the analyses. Descriptive statistics were used to investigate patient characteristics. Unless otherwise stated, data are shown as median (range). Proportions between groups were compared with chi-square tests, and nonparametric data were compared with Wilcoxon rank-sum tests. The area under the receiver operating characteristic curves (AUROCs) for the presence of a deranged physiologic parameter and critical NEWS were calculated. A multivariable logistic regression model was built to investigate independent associations with mortality. All parameters considered biologically plausible were included in the model and stepwise backward elimination was used to remove parameters at a significance level ($p = 0.20$). The final model included age, admitting specialty, admitting ward, intubation, and mechanical ventilation. When individual deranged physiologic parameters were analyzed, all the other deranged physiologic parameters were added to the model as potential confounders. Odds ratios (ORs) were given with a 95% CI, and p values were calculated using likelihood ratio tests. We

tested for collinearity by quantifying variance inflation factors. Single missing vital sign data were regarded as normal and sensitivity analysis, whereby the missing vital signs were excluded or regarded alternatively as deranged physiologic parameters, did not alter the results.

Ethical Considerations

Ethical clearance was granted by the National Institute for Medical Research in Tanzania (NIMR/HQ/R.8a/Vol.IX/1606), by Muhimbili University of Health & Allied Sciences (MU/DRP/AEC/Vol.XVI/125), and by the Swedish Ethical Review Board (EPN2015/673-31/2). Permission for the study was granted by The Tanzanian Commission for Science and Technology and by the Director of Medical Services at MNH. As the study was observational, was part of quality improvement on the ICU, and the data were anonymized for analysis, individual patient consent was waived by the ethics committees.

RESULTS

General Characteristics

Three hundred sixty patients were cared for in the ICU at

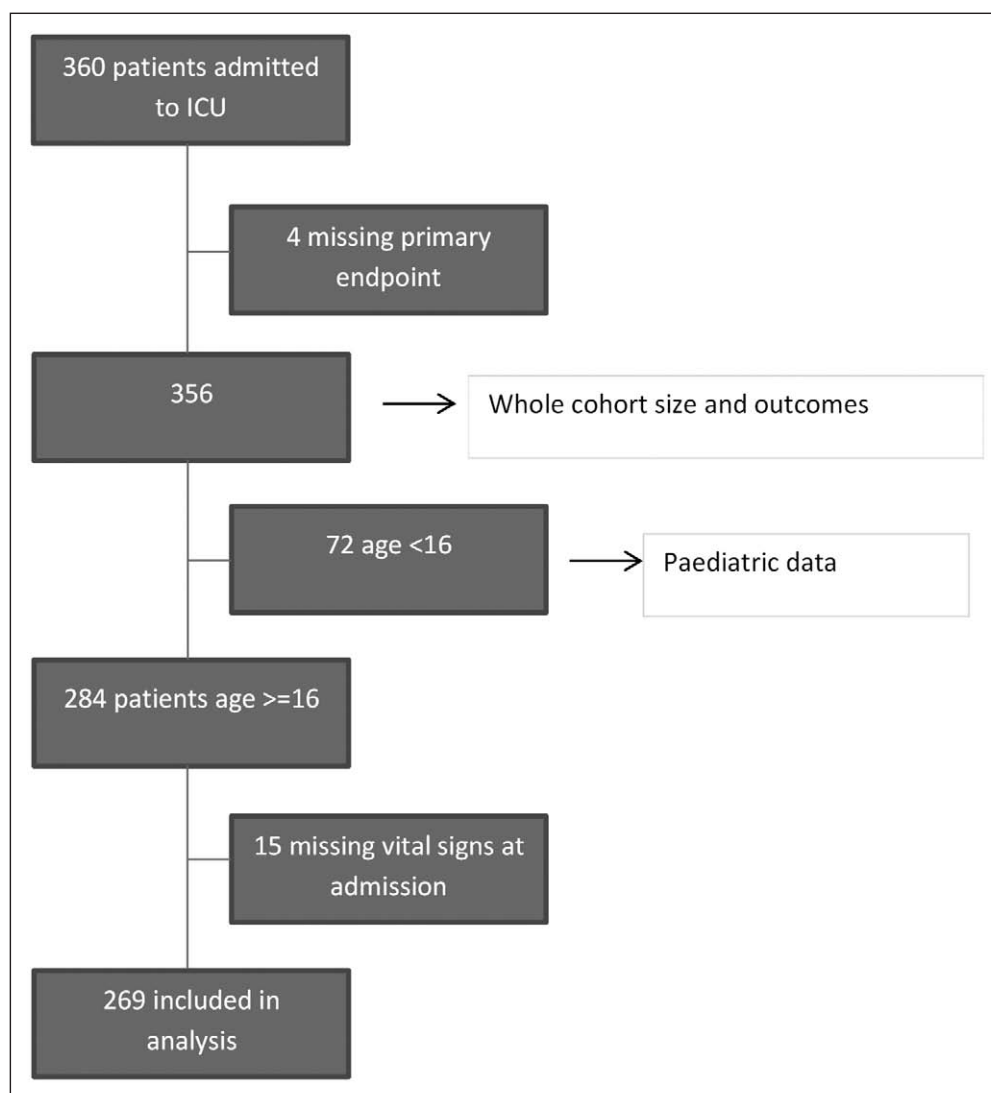


Figure 2. Study flowchart. Patients were admitted and had completed their care in the ICU between November 11, 2012 and March 10, 2014.

Muhimbili during the study period (Fig. 2). For the whole cohort, median age was 31 years (2 mo to 85 yr), ICU mortality was 46%, and in-hospital mortality was 51%.

Seventy-two of the patients were under 16 years old, median age 3 years (2 mo to 15 yr), ICU mortality of 45%, and an in-hospital mortality of 50%. Data on vital signs at admission were missing for 15 patients, 10 of whom died in hospital (60%). These two groups of patients were excluded from further analyses.

Of the remaining 269 patients, 54% were female with an average age of 35 years (16–85 yr) (Table 1). Patients were admitted from surgical specialties, obstetrics and gynecology, internal medicine, and infectious diseases. One quarter (26%) were planned admissions after elective surgery, and 113 (42%) were admitted following emergency surgery. One third (32%) were admitted without preceding surgery. Over half (59%) were admitted directly from the operating theater, and the other patients came from the hospital wards, the emergency room, and from other hospitals.

Illness Severity

At admission, 69% of patients had one or more deranged physiologic parameter (Table 2). Sixty-two percent had a critical NEWS greater than or equal to 7. The patients had a mean of 1.3 deranged physiologic parameters (range, 0–5) and a mean NEWS of 7.8 (0–18). The median length of stay (LOS) in the ICU was 1.8 days (30 min to 66 d), mortality within the first 24 hours was 14%, ICU mortality was 44%, and in-hospital mortality was 50%. Sixty-nine patients were planned admissions after elective surgery, 75% of these were still intubated but were not treated with mechanical ventilation (delayed extubation). The planned admissions had fewer deranged physiologic parameters at admission (mean, 0.3 [0–3]; $p < 0.001$), shorter LOS (0.9 d [0.7–15 d]; $p < 0.001$), and less in-hospital mortality (7%; $p < 0.001$) than the unplanned admissions (Table 2).

Deranged Physiologic Parameters as Prognostic Factors for Mortality

The distributions and mortality rates of deranged physiologic parameters, age, and vital signs can be seen in Figure 3. Sixty-four percent of the patients with a deranged physiologic parameter died in hospital compared with 18% without ($p < 0.001$). The presence of a deranged physiologic parameter at admission was associated with mortality (adjusted OR, 4.64 [1.95–11.09]; $p < 0.001$; AUROC, 0.70 [0.65–0.75]) (Table 3). Mortality increased with increasing number of deranged physiologic parameters (adjusted OR per increase of one deranged physiologic parameter, 2.24 [1.53–3.26]; $p < 0.001$).

Every individual deranged physiologic parameter was associated with mortality with statistically significant unadjusted ORs between 1.92 and 16.16 (Table 3). Collinearity between the deranged physiologic parameters was not high (all variance inflation factors were < 10). Deranged physiologic parameters for GCS, respiratory rate, and systolic blood pressure remained significant after adjusting. Systolic blood pressure less than 90 mm Hg had the largest OR. Severe hypothermia (body temperature $\leq 35.1^\circ\text{C}$) (OR, 0.30 [0.04–2.61]; $p = 0.28$), severe hyperthermia

TABLE 1. Age, Sex, Admitting Ward, Admitting Specialty, and Respiratory Support at Admission for All Patients Over 16 Years Old

Characteristic	Adults ≥ 16 Yr ($n = 269$) n (%)
Age, median (range) in yr	35 (16–85)
Female	146 (54)
Admitted to ICU from	
Ward in Muhimbili Hospital	53 (20)
Emergency department	48 (18)
Operating theater	160 (59)
Other hospital	8 (3)
Planned admissions	
Postoperative elective surgery	69 (26)
ENT	37 (14)
Thyroid	16 (6)
Abdominal	7 (3)
Thoracic	9 (3)
Unplanned admission	200 (74)
Postoperative emergency surgery	
Any emergency surgery	113 (42)
Abdominal	68 (25)
ENT	5 (2)
Obstetrics/gynecology	30 (11)
Thyroid	2 (0.7)
Breast	1 (0.4)
Urological/renal	2 (0.7)
Thoracic	5 (2)
Medical ^a	87 (32)
Obstetrics/gynecology	12 (4)
Internal medicine	52 (19)
Infectious diseases	17 (6)
Foreign body/poisoning	5 (2)
Unknown	1 (0.4)
Receiving oxygen	221 ^b (88)
Intubated	202 (75)
Mechanical ventilation	137 (51)

ENT = ear, nose, and throat.

^aMedical = not postoperative.

^bData missing on oxygen therapy at admission for 19 patients.

(body temperature $\geq 39.1^\circ\text{C}$) (OR, 1.09 [0.44–2.68]; $p = 0.85$), and hypertension (systolic blood pressure > 180) (OR, 0.67 [0.06–7.49]; $p = 0.74$) were not associated with mortality.

TABLE 2. Illness Severity at Admission, Mortality Rates, and Length of Stay in the ICU, Grouped Into Planned and Unplanned Admissions

Parameter	All (n = 269), n (%)	Planned Admissions (n = 69), n (%)	Unplanned Admissions (n = 200), n (%)	p
Deranged physiologic parameters				
Patients without any deranged physiologic parameters	83 (31)	49 (71)	34 (17)	< 0.001 ^a
Patients with one or more deranged physiologic parameter	186 (69)	20 (29)	166 (83)	
No. of deranged physiologic parameters, mean (range)	1.3 (0–5)	0.3 (0–3)	1.6 (0–5)	< 0.001 ^b
NEWS				
Patients with NEWS < 7	101 (38)	43 (62)	58 (29)	< 0.001 ^a
Patients with NEWS ≥ 7	168 (62)	26 (38)	142 (71)	
NEWS, mean (range)	7.8 (0–18)	6.1 (0–12)	8.3 (0–18)	< 0.001 ^b
Mortality rates				
24-hr mortality	39 (14)	1 (1)	38 (19)	< 0.001 ^a
ICU mortality	119 (44)	3 (4)	116 (58)	< 0.001 ^a
In-hospital mortality	134 (50)	5 (7)	129 (65)	< 0.001 ^a
Length of stay in ICU, median (range), d	1.8 (0.02–66)	0.9 (0.7–15)	2.7 (0.02–66)	< 0.001 ^b

NEWS = National Early Warning Score.

^ap values compare groupings by chi-square test for proportions.

^bp values compare groupings by Wilcoxon rank-sum test for nonparametric data.

Other Factors and Mortality

Increasing age was associated with mortality (adjusted OR, 1.03 per yr [1.01–1.06]; $p = 0.003$) as was the use of mechanical ventilation at admission (adjusted OR, 3.46 [1.15–10.42]; $p = 0.03$), but gender was not (OR, 0.71 [0.44–1.48]; $p = 0.16$). A critical NEWS of greater than or equal to 7 had an association with mortality (adjusted OR, 2.51 [1.23–5.14]; $p = 0.01$; AUROC, 0.64 [0.58–0.69]) (Table 3).

Early Deaths

Twenty-four patients (9%) died within 12 hours of admission to ICU. All of these patients were unplanned admissions and they had a heterogeneous range of diagnoses. Their median age was 36.5 years (range, 19–73 yr) and 54% were female. All of them had at least one deranged physiologic parameter at admission and they had more deranged physiologic parameters (2.4 [1–5]) than the other patients (1.2 [0–5]; $p < 0.001$).

DISCUSSION

Deranged Physiologic Parameters

We have found that the presence of a deranged physiologic parameter can be used as a measure of illness severity in a critically ill population in a low-income country. A deranged physiologic parameter at admission to ICU was strongly associated with in-hospital mortality. Furthermore, the risk of in-hospital death increased with an increasing number of deranged physiologic parameters. These findings are consistent with the results in a previous study looking at the

association of deranged vital signs at admission to hospital in Tanzania with death (20).

Individual Deranged Physiologic Parameters

All the individual deranged physiologic parameters had an unadjusted association with mortality while body temperature and hypertension did not. This gives some validation to the design of our deranged physiologic parameter model. Hypotension (systolic blood pressure < 90 mm Hg) had the strongest association and remained significant after adjusting for confounders. Ninety-two percent of patients with hypotension died in hospital. Systolic blood pressure has recently been shown to be associated with early mortality in trauma patients in India (21). International recommendations for shock include early identification and fluid resuscitation (22, 23), and a recent intervention study of sepsis in Uganda reduced mortality from 45.7% to 33.0% using monitoring and fluid resuscitation (24). Our results suggest that this could be a possible area for improvement on the unit.

Comparison With NEWS

Our results suggest that in this setting, for an association with mortality, single deranged physiologic parameters are as useful as the more complex NEWS compound scoring system. One previous study has found that compound scores were better than single parameters for discriminating the risk of adverse outcomes (25). However, the authors also concluded that “there may be a case for defining extreme values for each vital sign ... irrespective of the aggregate NEWS score” and the NEWS protocol in use throughout

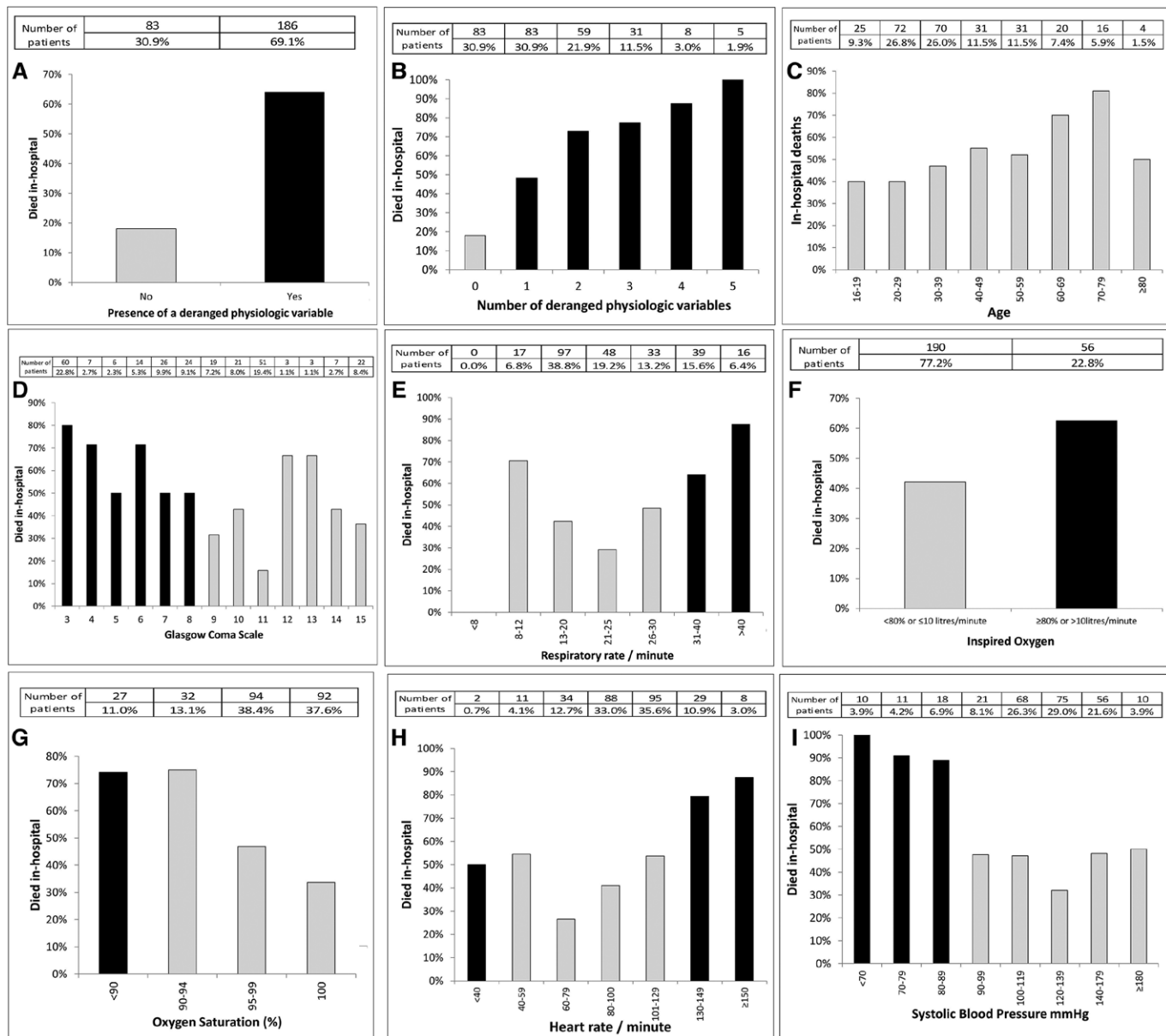


Figure 3. In-hospital mortality rates by presence of a deranged physiologic parameter (A), number of deranged physiologic parameters (B), age (C), Glasgow Coma Scale (GCS) (D), respiratory rate (E), inspired oxygen (F), oxygen saturation (G), heart rate (H), and systolic blood pressure (I) at admission. Missing vital signs excluded from graphs. *Black bars* represent deranged physiologic parameters and *gray bars* represent normal.

the United Kingdom includes escalation of care when single “red signs” are discovered (19).

Prognostic Factors

The aim of our study was to investigate whether single deranged physiologic parameters are prognostic factors for mortality and not to find the best-fitting multivariable prediction model. Single parameters are simple and quick to evaluate, making them pragmatic for settings with low staffing levels, such as in hospitals in Tanzania. While multivariable models have shown good results in some settings (12, 26), their usefulness has been questioned—Early Warning Scores were not accurate enough for clinical use in Malawi (27) or in Canada (28). Single deranged physiologic parameters have the added benefit of indicating which vital function is failing, allowing a direct link to a protocol advising

a treatment modification, which a compound score does not. A deranged physiologic parameter for hypotension, for example, can be followed by an instruction to administer fluid. Following this study, MNH is introducing a protocol on the ICU that uses this methodology.

Mortality Rates

We have described a patient cohort on a mixed ICU in a low-income country. An in-hospital mortality rate of 50% and ICU mortality rate of 44% for all patients greater than or equal to 16 years old (65% and 58% respectively for unplanned patients) are strikingly high, especially given the young age of the patients. Similar figures were found in a recent survey of four ICUs in Tanzania including Muhimbili (29). A worldwide survey of ICUs in 2014 found an in-hospital mortality of 22.4% (30). There are two

TABLE 3. Mortality and Association With Physiologic Derangements at Admission

Physiologic Derangement	In-Hospital Mortality				ORs (95% CI)	
	Without the Derangement		With the Derangement		Unadjusted	Adjusted
	n ¹ /n ²	%	n ¹ /n ²	%		
One or more deranged physiologic parameter	15/83	18.0	119/186	64.0 ^{ab}	8.05 (4.27–15.18) ^a	4.64 (1.95–11.09) ^{ac}
National Early Warning Score ≥ 7	32/101	31.7	102/168	60.7 ^{ab}	3.33 (1.97–5.61) ^a	2.51 (1.23–5.14) ^{cd}
Conscious level (Glasgow Coma Scale score ≤ 8)	43/132	32.6	91/137	66.4 ^{ab}	4.09 (2.46–6.8) ^a	2.27 (1.03–5.04) ^{de}
Respiratory rate (< 8 or > 30/min)	95/214	44.4	39/55	70.9 ^{ab}	3.05 (1.61–5.80) ^d	3.01 (1.13–7.99) ^{de}
Inspired oxygen (≥ 80% or ≥ 10L/min)	99/213	46.5	35/56	62.5 ^{bd}	1.92 (1.05–3.51) ^d	0.84 (0.30–2.31) ^e
Oxygen saturation (< 90%)	114/242	47.1	20/27	74.1 ^{bd}	3.21 (1.31–7.87) ^d	1.53 (0.44–5.37) ^e
Heart rate (< 40 or > 130/min)	104/232	44.8	30/37	81.1 ^{ab}	5.27 (2.22–12.50) ^a	2.01 (0.65–6.20) ^e
Systolic blood pressure (< 90 mm Hg)	98/230	42.6	36/39	92.3 ^{ab}	16.16 (4.83–54.01) ^a	32.55 (7.01–151.04) ^{ae}

n¹ = number of patients that died, n² = number of patients, ORs = odds ratios.

^ap < 0.001.

^bChi-square test.

^cAdjustments for age, admitting specialty, admitting ward, intubation, and mechanical ventilation.

^dp < 0.05.

^eAdjustments for age, admitting specialty, admitting ward, intubation, and mechanical ventilation and all other individual deranged physiologic parameters.

In-hospital mortality and associations with physiologic derangements at admission expressed as the presence of a deranged physiologic parameter, a critical National Early Warning Score, and each individual deranged physiologic parameter.

Odds ratios calculated with unadjusted and multivariable logistic regression.

potential explanations for the high mortality rates in our study: a very sick patient selection or poor quality of care on the unit. The level of physiologic derangement at admission may support the first explanation: 83% of unplanned admissions had one or more deranged physiologic parameters, average 1.6 per patient. Furthermore, 24 patients (9%) died within 12 hours of admission—it is likely that a large proportion of these patients were not salvageable. In a 1,500-bedded hospital, such as Muhimbili, it would be expected that far more patients would be critically ill than the six-bedded ICU could admit. Furthermore, the short median LOS of 1.8 days for 360 patients over a 15-month period indicates that the ICU beds were not continuously occupied. Although the ICU has official admission criteria based on failing vital organ systems, many such patients who could benefit from intensive care are treated in other parts of the hospital. Whether the de facto admission criteria were an extreme severity of illness or other factors was not possible for us to study: we did not gather data on the specific reasons for admission for the patients or their comorbidities. However, we are also aware that the unit lacks both resources for good quality intensive care and routines for managing patients with physiologic derangement (3, 10).

Measuring Illness Severity

Measuring the severity of illness of ICU patients and populations is important for triage and patient selection. Intensive care is a limited resource in all countries in the world, and allocating

these resources to the people who will most benefit is vital. Both patients who are too healthy and those who are too sick are not good candidates for intensive care and should be cared for in general wards or palliative care units, respectively. Resource allocation is especially relevant in low-income countries (31). A high ICU mortality rate such as that in our study makes for a tremendously challenging working environment that could risk staff burnout, fatalism, and potentially salvageable patients could be missed (32).

Measuring illness severity also enables comparisons between units and for evaluating quality of care. Scores such as Acute Physiology and Chronic Health Evaluation (33), Simplified Acute Physiology Score (34), and Sequential Organ Failure Assessment (35) have been developed in high-income countries to enable the calculation of standardized mortality rates and benchmarking. They cannot be used in ICUs in low-income countries due to the lack of advanced monitoring and laboratory testing. A vital signs–based system was developed in Zambia in 1989 but has not been widely adopted (36). There have been calls for registries of intensive care facilities and performance in low- and middle-income countries to improve access and quality (37). Deranged physiologic parameters could potentially be used for both patient selection and quality comparisons.

Strengths

As far as we are aware, our findings are the first to suggest that single deranged physiologic parameters could be used

to identify at-risk patients and to trigger treatment modifications in an ICU in a low-income country. Such routines have become standard practice in ICUs and many general wards in high-income countries (13). Our prospective study design minimized missing data and the international collaboration within which the study was embedded strengthened communication and logistics.

Limitations

The study is single centered and was based in a large, university hospital in Tanzania. Generalizing the results to settings with fewer resources, such as small district hospitals, or to those with greater resources, such as hospitals in high-income countries, should be done with caution. Our findings of strong associations with mortality should not be interpreted as predictions for individual patients. The presence of a deranged physiologic parameter does not predict that the patient will die, and the absence of a deranged physiologic parameter does not predict survival. As biology and pathologies are so heterogeneous, it is unlikely that predictive models based on simple vital signs can have sufficient predictive value. As we were not directly observing care, we were not able to assess the reliability of the documentation on the unit. However, only 5.3% of patients were excluded due to a lack of vital signs at admission, and we do not have reason to believe that documentation was inconsistent or unreliable.

Further Research

Further research is warranted to understand patient selection to ICUs in low-income countries and to investigate whether it is feasible to introduce routines whereby emergency treatment modifications triggered by deranged physiologic parameters can improve the quality of care and outcomes for critically ill patients when resources are limited.

CONCLUSION

Single deranged physiologic parameters at admission are associated with mortality in a critically ill population in a low-income country and could be termed “danger signs.” Danger signs may be suitable for the basis of routines to identify and treat critically ill patients.

ACKNOWLEDGMENTS

We thank the research assistants Agness Laizer, Erasto Kalinga, Elizabeth Stephens, Nazahed Richards, Ulrica Mickelsson, and Lotta Förars. We also thank Gaetano Marrone and Ulf Larsson for statistical consultancy.

REFERENCES

- Adhikari NK, Fowler RA, Bhagwanjee S, et al: Critical care and the global burden of critical illness in adults. *Lancet* 2010; 376:1339–1346
- Fowler RA, Adhikari NK, Bhagwanjee S: Clinical review: Critical care in the global context—Disparities in burden of illness, access, and economics. *Crit Care* 2008; 12:225
- Baelani I, Jochberger S, Laimer T, et al: Availability of critical care resources to treat patients with severe sepsis or septic shock in Africa: A self-reported, continent-wide survey of anaesthesia providers. *Crit Care* 2011; 15:R10
- Dünser MW, Baelani I, Ganbold L: A review and analysis of intensive care medicine in the least developed countries. *Crit Care Med* 2006; 34:1234–1242
- Jacob ST, Moore CC, Banura P, et al; Promoting Resource-Limited Interventions for Sepsis Management in Uganda (PRISM-U) Study Group: Severe sepsis in two Ugandan hospitals: A prospective observational study of management and outcomes in a predominantly HIV-1 infected population. *PLoS One* 2009; 4:e7782
- Ilori IU, Kalu QN: Intensive care admissions and outcome at the University of Calabar Teaching Hospital, Nigeria. *J Crit Care* 2012; 27:105.e1–105.e4
- Towey RM, Ojara S: Practice of intensive care in rural Africa: An assessment of data from Northern Uganda. *Afr Health Sci* 2008; 8:61–64
- Gombar S, Ahuja V, Jafra A: A retrospective analysis of obstetric patient's outcome in intensive care unit of a tertiary care center. *J Anaesthesiol Clin Pharmacol* 2014; 30:502–507
- WHO: World Health Statistics. Geneva, WHO, 2014
- Baker T, Lugazia E, Eriksen J, et al: Emergency and critical care services in Tanzania: A survey of ten hospitals. *BMC Health Serv Res* 2013; 13:140
- Bleyer AJ, Vidya S, Russell GB, et al: Longitudinal analysis of one million vital signs in patients in an academic medical center. *Resuscitation* 2011; 82:1387–1392
- Smith GB, Prytherch DR, Meredith P, et al: The ability of the National Early Warning Score (NEWS) to discriminate patients at risk of early cardiac arrest, unanticipated intensive care unit admission, and death. *Resuscitation* 2013; 84:465–470
- Winters BD, Weaver SJ, Pfoh ER, et al: Rapid-response systems as a patient safety strategy: A systematic review. *Ann Intern Med* 2013; 158:417–425
- Peake SL, Delaney A, Bailey M, et al: Goal-directed resuscitation for patients with early septic shock. *N Engl J Med* 2014; 371:1496–1506
- Andrews B, Muchemwa L, Kelly P, et al: Simplified severe sepsis protocol: A randomized controlled trial of modified early goal-directed therapy in Zambia. *Crit Care Med* 2014; 42:2315–2324
- Bell MB, Konrad D, Granath F, et al: Prevalence and sensitivity of MET-criteria in a Scandinavian University Hospital. *Resuscitation* 2006; 70:66–73
- Bellomo R, Goldsmith D, Uchino S, et al: A prospective before-and-after trial of a medical emergency team. *Med J Aust* 2003; 179:283–287
- Konrad D, Jäderling G, Bell M, et al: Reducing in-hospital cardiac arrests and hospital mortality by introducing a medical emergency team. *Intensive Care Med* 2010; 36:100–106
- RCP: National Early Warning Score (NEWS). Standardising the Assessment of Acute-Illness Severity in the NHS. Report of a Working Party. London, Royal College of Physicians, 2012
- Rylance J, Baker T, Mushi E, et al: Use of an early warning score and ability to walk predicts mortality in medical patients admitted to hospitals in Tanzania. *Trans R Soc Trop Med Hyg* 2009; 103:790–794
- Gerdin M, Roy N, Khajanchi M, et al: Predicting early mortality in adult trauma patients admitted to three public university hospitals in urban India: A prospective multicentre cohort study. *PLoS One* 2014; 9:e105606
- Dünser MW, Festic E, Dondorp A, et al; Global Intensive Care Working Group of European Society of Intensive Care Medicine: Recommendations for sepsis management in resource-limited settings. *Intensive Care Med* 2012; 38:557–574
- Cecconi M, De Backer D, Antonelli M, et al: Consensus on circulatory shock and hemodynamic monitoring. Task force of the European Society of Intensive Care Medicine. *Intensive Care Med* 2014; 40:1795–1815
- Jacob ST, Banura P, Baeten JM, et al; Promoting Resource-Limited Interventions for Sepsis Management in Uganda Study Group: The impact of early monitored management on survival in hospitalized adult Ugandan patients with severe sepsis: A prospective intervention study. *Crit Care Med* 2012; 40:2050–2058

25. Jarvis S, Kovacs C, Briggs J, et al: Aggregate National Early Warning Score (NEWS) values are more important than high scores for a single vital signs parameter for discriminating the risk of adverse outcomes. *Resuscitation* 2015; 87:75–80
26. Opio MO, Nansubuga G, Kellett J: Validation of the VitalPAC™ Early Warning Score (VIEWS) in acutely ill medical patients attending a resource-poor hospital in sub-Saharan Africa. *Resuscitation* 2013; 84:743–746
27. Wheeler I, Price C, Sitch A, et al: Early warning scores generated in developed healthcare settings are not sufficient at predicting early mortality in Blantyre, Malawi: A prospective cohort study. *PLoS One* 2013; 8:e59830
28. Murray A, Kellett J, Huang W, et al: Trajectories of the averaged abbreviated Vitalpac early warning score (AbEWS) and clinical course of 44,531 consecutive admissions hospitalized for acute medical illness. *Resuscitation* 2014; 85:544–548
29. Sawe HR, Mfinanga JA, Lidenge SJ, et al: Disease patterns and clinical outcomes of patients admitted in intensive care units of tertiary referral hospitals of Tanzania. *BMC Int Health Hum Rights* 2014; 14:26
30. Vincent JL, Marshall JC, Namendys-Silva SA, et al; ICON investigators: Assessment of the worldwide burden of critical illness: The intensive care over nations (ICON) audit. *Lancet Respir Med* 2014; 2:380–386
31. Riviello ED, Letchford S, Achieng L, et al: Critical care in resource-poor settings: Lessons learned and future directions. *Crit Care Med* 2011; 39:860–867
32. Chimwaza W, Chipeta E, Ngwira A, et al: What makes staff consider leaving the health service in Malawi? *Hum Resour Health* 2014; 12:17
33. Knaus WA, Wagner DP, Draper EA, et al: The APACHE III prognostic system. Risk prediction of hospital mortality for critically ill hospitalized adults. *Chest* 1991; 100:1619–1636
34. Le Gall JR, Lemeshow S, Saulnier F: A new Simplified Acute Physiology Score (SAPS II) based on a European/North American multicenter study. *JAMA* 1993; 270:2957–2963
35. Vincent JL, de Mendonça A, Cantraine F, et al: Use of the SOFA score to assess the incidence of organ dysfunction/failure in intensive care units: Results of a multicenter, prospective study. Working group on “sepsis-related problems” of the European Society of Intensive Care Medicine. *Crit Care Med* 1998; 26:1793–1800
36. Watters DA, Wilson IH, Sinclair JR, et al: A clinical sickness score for the critically ill in Central Africa. *Intensive Care Med* 1989; 15:467–470
37. Dondorp AM, Haniffa R: Critical care and severe sepsis in resource poor settings. *Trans R Soc Trop Med Hyg* 2014; 108:453–454