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Clinical paper

Oxygen use in low-resource settings: An intervention still triggered by intuition

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Abstract

Background: Although hypoxic patients attending low-resource hospitals have a high mortality, many are not given supplemental oxygen. If oximetry is not available, then the decision to provide oxygen must be based on other factors.

Methods: The variables associated with the decision to provide supplemental oxygen made by an emergency department staff, without access to oximetry, in a low resource Ugandan hospital were determined from data collected within 16h of admission to the hospital's medical and surgical wards.

Results: Of 2,599 patients, 731 (28.1%) had an oxygen saturation <95%, and 164 (6.3%) an oxygen saturation <90%. Of the 731 patients with oxygen levels below 95% 573 (83%) were not given oxygen; oxygen was only given to 63 (38%) of the 164 patients with oxygen saturation <90%. On average, a patient given oxygen was more likely to die than one not given oxygen, regardless of their oxygen saturation (odds ratio 13.4, 95%CI 9.1−19.6). After multivariate analysis weakness, dyspnoea, low oxygen saturation, high heart rate, high respiratory rate, low temperature, alertness, gait, and a medical illness were all significantly associated with the use of supplemental oxygen and in-hospital mortality. Logistic regression modelling of these variables had comparable discrimination for both oxygen use (c statistic 0.88 SE 0.02) and in-hospital mortality (c statistic 0.84 SE 0.02).

Conclusion: The intuitive decision to provide oxygen was strongly associated with in-hospital mortality, suggesting that oxygen was given to those considered the sickest patients. In the future, oximetry may guide oxygen therapy more efficiently.

Keywords: Intuition, Supplemental oxygen, Emergency care, Acute medical care, Low resource settings, In-hospital mortality

Introduction

The presence of hypoxia is a well-recognised predisposing factor for adverse events, such as tachycardia, periodic breathing, "mountain sickness", impaired memory, fainting, loss of consciousness,[1] intensive care admission[2] and in-hospital mortality.[3] Prior to the availability of oximetry hypoxia was assessed by breathlessness, respiratory distress, cyanosis, vital sign changes and altered consciousness.[4] However, for acutely ill patients without chronic lung disease there is no clear correlation between physical signs and symptoms and oxygenation.[5] At atmospheric pressure normal oxygen saturation is greater than 95%, and most guidelines recommend supplemental oxygen in acutely ill patients to maintain an oxygen saturation level over 94%, with lower levels for those with chronic obstructive lung disease.[6] However, the normal range for oxygen saturation varies according to patient age, and a saturation of 92% may be normal for 70year old patients[7] and many authors use 90% as a cut-off for clinically significant hypoxia.[3,4,8] Whilst in an emergency resuscitation the empiric administration of oxygen is often life-saving, a large meta-analysis has reported that oxygen saturation levels above 96% are harmful and that prolonged supplemental oxygen should not be used above this

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level.[9] Moreover, although there is a widespread and longstanding custom of giving oxygen for palliation to sick patients regardless of their blood oxygen saturation[6] there is no evidence that oxygen relieves breathlessness in patients who are not hypoxic.[10]

Although effective and efficient care is possible,[11] the need for emergency care in low income countries has been neglected as health policies focus on communicable diseases and maternal child health.[12] Of the 29 countries listed by the World Bank as low-income (i.e. per capita annual income less than US$1,035), 22 of them, including Uganda, are in sub-Saharan Africa.[13] For many patients in these countries supplemental oxygen is unaffordable.[14] Moreover, Sir William Osler's belief that the use of supplemental oxygen "foretold a fatal prognosis"[15] persists in Uganda, where many patients refuse oxygen treatment, or only consent to it when they are *in extremis,* as they believe it to be a harbinger of death.[16] In addition, the need for oxygen treatment on admission is usually determined after a rapid intuitive assessment without the aid of oximetry by a recently qualified doctor in training.

The purpose of this study was to identify the factors that might influence the use of supplemental oxygen, and if patients might benefit if it were guided by oximetry: it was not to develop or validate a robust predictive score for either oxygen use or in-hospital mortality.

Methods

Aim

to determine the variables associated with the use of supplemental oxygen guided by intuitive clinical assessment without oximetry in a low-resource hospital in a low-income country,[13] and their relationship to in-hospital mortality.

Study design and setting

This retrospective observational non-interventional study was performed on a 46-bed medical ward at Kitovu Hospital, which has 220 beds and is located near Masaka, Uganda, 140 km from the capital city of Kampala. It is a Private Not for Profit (PNFP) Hospital, operated by the Uganda Catholic Medical Bureau. The average charge for a medical admission is US$60, and the income of most patients attending the hospital would be below the average Ugandan per capita annual income of US$1,035.[13] Currently, the hospital has no full-time specialist physician and most emergency medical care is provided by unsupervised doctors in training. The hospital has no blood gas analysis machine, no intensive care unit, and cannot provide assisted ventilation or renal dialysis. We believe these resources are like those of many hospitals throughout sub-Saharan Africa.

Participants and data collection

From 26th May 2018 to 29th June 2020 the clinical status and vital signs on admission of every patient admitted to the hospital's medical unit were entered at the bedside using tablet computers into a clinical data management and decision support system (rapid electronic assessment data system [READS], Tapa Healthcare DAC) by three dedicated nurse researchers, who worked in shifts from 9am to 5pm 7-days-a-week.

On the 17th March 2019, the system was expanded to the hospital's surgical ward. Data were entered twice a day (i.e. morning and evening). Therefore, there could have been a delay of up to 16 h between admission to the ward and vital signs being measured.

All patients arrived at the hospital for emergency assessment, and none arrived by appointment or electively. None of the patients were elective admissions, and no patients were excluded from the study (apart from surgical patients admitted prior to 17th March 2019). All patients were initially assessed in the emergency department, which does not have access to an oximeter. The nearby medical ward has one oxygen cylinder and two oxygen concentrators, which are available if not already in use.

READS requires that the patient's contemporaneous mental alertness, mobility, and complaints to be entered each time the vital signs are measured. This structured bedside assessment requires the recording of pain by site and severity, breathlessness, bleeding, as well as vomiting and diarrhoea. Based on analysis of data previously collected by the system a revised version of the assessment was introduced in May 2018, which included the patients' subjective feelings of improvement, feelings of weakness, mid-upper arm circumference (MUAC), suspicion of stroke, and HIV status (hospital policy is that all admitted patients should be tested). The patient's status at discharge (i.e. dead or alive) was also recorded in the system. In total the system currently collects 20 items of data at each assessment. Data entry into the READS system was automatically time and date stamped: there was no missing data as it was impossible to complete a READS assessment without entering all the data required, or to enter values that was outside a plausible range, or to close the assessment without entering the patient's condition at hospital discharge (i.e. dead or alive).

Oxygen saturation was measure from the finger by the Acc-U Rate CMS 500D oximeter (CMS Mobility Inc., Stafford, Texas, USA). A period from 30 to 60 s was required to obtain a stable pulse and oxygen saturation reading. Impaired mobility on presentation was defined in both cohorts as lack of a stable independent gait when first assessed. Therefore, any patients that were unsteady on their feet, needed a walking stick or other aid to steady themselves, needed help to walk, or were bedridden were considered to have an unstable gait. A patient who was not alert, attentive, calm, and coherent was recorded as "not alert". HIV status was recorded as known to be negative, positive, or unknown. A feeling of improvement was recorded as "feeling better" or "no improvement".

Statistical methods and data analysis

All the 20 variables collected at the first READS assessment after admission were analysed. The variables significantly associated with supplemental oxygen and in-hospital mortality were identified by univariate analysis. Logistic regression identified those symptoms and/or signs with odds ratios that remained significantly associated with supplemental oxygen when adjusted for the presence of all the other variables identified to be significantly associated with supplemental oxygen by univariate analysis.

Calculations were performed using Epi-Info version 6.0 (Centre for Disease Control and Prevention, USA). Numeric variables were compared using Student's t-test and categorical variables were compared using Chi square analysis with Yates continuity correction when applicable. The optimal cut-off to convert continuous variables into a categorical variable was the value with the highest Chi-square for supplemental oxygen use. Adjustment of odds ratios by stepwise logistic regression analysis was performed using Logistic software.[17] The c statistic was used to assess the discrimination of predictive models according to the method of Hanley and McNeil.[18] The p value for statistical significance was 0.05.

Ethics

Ethical approval of the study was obtained from the Scientific Ethics Committee Kitovu Hospital. The study conforms to the principles outlined in the Declaration of Helsinki.[19] The study is reported in accordance with the STROBE statement.[20]

Results

The number of patients given and not given supplemental oxygen

Out of 2599 patients admitted 731 (28.1%) had an oxygen saturation <95%, and 164 (6.3%) an oxygen saturation <90%. A total of 214 (8.2%) patients were given supplemental oxygen. Of the 731 patients with oxygen levels below 95% 573 (83%) were not given oxygen: oxygen was only given to 63 (38%) of the 164 patients with oxygen saturation <90%.

Outcomes of patients given and not given supplemental oxygen

Of the 214 patients given oxygen 122 (57%) had an oxygen saturation ≥95%, and 63 (29.4%) a level ≥90% (Fig. 1). All the patients given oxygen were more likely to die than those not given oxygen, regardless of their oxygen saturation (Table 1a). There was no difference in the mortality of patients with an oxygen saturation from 90 to 94% given oxygen compared to those given oxygen with saturations ≥95%. Similarly, patients not given oxygen with saturations from 90 to 94% had the same mortality as those not given oxygen with saturations ≥95% (Table 1b).

Variables associated with supplemental oxygen use

Patients given oxygen were older, had faster heart and respiratory rates, and lower oxygen saturations and mid-upper arm circumference than those not given oxygen: there was no difference in the length of hospital stay between those given and not given oxygen (6.2 SD 5.8 versus 5.7 SD 5.3 days, p 0.26). The optimal Chi-square determined "cut-off" values for supplemental oxygen use were determined for vital signs and other continuous variables (Table 2).

Of the 20 variables available and/or routinely collected at bedside assessment, only active pain, vomiting, diarrhoea, and bleeding were not associated with supplemental oxygen use (Table 3). Apart from female gender, all the variables associated with supplemental oxygen use were also significantly associated with in-hospital mortality. However, the strongest association with in-hospital mortality of all the variables tested was the use of supplemental oxygen (odds ratio 13.4, 95%CI 9.06−19.72, Chi-square 282.7) (see supplemental data).

Weakness, dyspnoea, oxygen saturation, heart and respiratory rate, temperature, alertness, gait, and a medical illness retained their statistically significant association with in-hospital mortality after adjustment by logistic regression. A predictive model, which assigned one point for every variable's logistic regression coefficient to the nearest integer (Table 4) had a c statistic for the use of supplemental oxygen of 0.88 SE 0.02 and 0.84 SE 0.02 for in-hospital mortality; these were not statistically different (p=0.10) and the probability of supplemental oxygen use and in-hospital mortality rose together with each point of the score (Fig. 2).

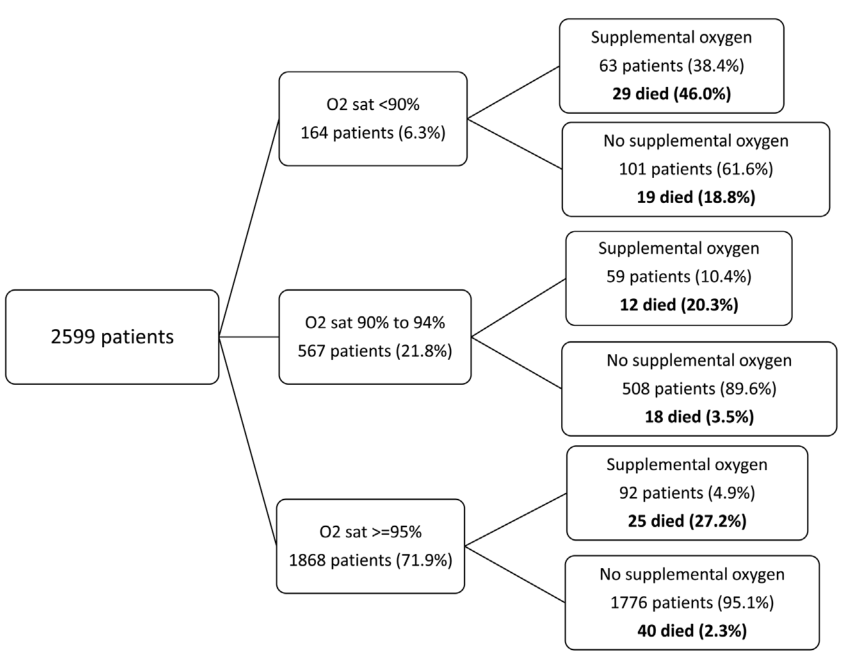

Fig. 1 – Patients in study according to oxygen saturation on admission, provision of supplemental oxygen, and in-hospital mortality. O2 sat=oxygen saturation.

Table 1a – Odds ratio for in-hospital mortality between patients given and not give oxygen according to their oxygen saturation levels on admission.

	Pt No.	In-hospital mortality	Pt No.	In-hospital mortality	Odds ratio	(0.95% CI)	Chi-square	p
	Oxygen given		Oxygen not given					
O2 sat <90%	63	46.0%	101	18.8%	3.68	(1.72 7.92)	12.60	<.0001
O2 sat <95%	122	33.6%	609	6.1%	7.83	(4.60 13.33)	77.96	<.0001
O2sat 90%–94%	59	20.3%	508	3.5%	6.95	(2.94 16.33)	26.50	<.0001
O2sat ≥95%	92	27.2%	1776	2.3%	16.19	(8.95 29.25)	154.42	<.0001
All patients	214	30.8%	2385	3.2%	13.37	(9.10 19.64)	282.69	<.0001

O2sat, oxygen saturation on admission.

Table 1b – Odds ratio for in-hospital mortality between patients according to their oxygen saturation levels on admission and if they were given supplemental oxygen.

	Pt No.	In-hospital mortality	Pt No.	In-hospital mortality	Odds ratio	(0.95% CI)	Chi-square	p
	O2sat <90%		O2sat 90%–94%					
Oxygen given	63	46.0%	59	20.3%	3.34	(1.39 8.11)	17.90	0.005
Oxygen not given	101	18.8%	508	3.5%	6.31	(3.02 13.20)	31.80	<.0001
	O2sat 90%–94%		O2sat ≥95%					
Oxygen given	59	20.3%	92	27.2%	0.68	(0.29 1.60)	0.58	0.45
Oxygen not given	508	3.5%	1776	2.3%	1.59	(0.87 2.89)	2.16	0.14
	O2sat <90%		O2sat >=95%					
Oxygen given	63	46.0%	92	27.2%	2.29	(1.10 4.76)	5.06	0.02
Oxygen not given	101	18.8%	1776	2.3%	10.06	(5.35 18.80)	80.72	<.0001
	O2sat <90%		O2sat ≥90%					
Oxygen given	63	46.0%	151	24.5%	2.63	(1.34 5.15)	8.68	0.003
Oxygen not given	101	18.8%	2284	2.5%	8.89	(4.84 16.22)	76.85	<.0001

O2sat, oxygen saturation on admission.

Table 2 – Differences in continuous variables between those given and not given supplemental oxygen, and the "cut off" value that converts each variable to a categorical variable with the highest Chi-square value.

Variable	All patients	Supplemental oxygen: Not given (n 2385)	Supplemental oxygen: Given (n 214)	p	Chi-square determined "Cut-off"
Age (years)	48.7 SD 22.8	48.0 SD 22.6	56.1 SD 24.3	<0.00001	>64 years
Heart rate (bpm)	87 SD 20	86 SD 19	98 SD 26	<0.00001	>114 bpm
Respiratory rate (bpm)	22 SD 6	21 SD 5	28 SD 9	<0.00001	>27 bpm
Temperature (°C)	36.4 SD 0.6	36.4 SD 0.6	36.5 SD 0.8	0.69	<36.1°C
Oxygen saturation (%)	95 SD 7	95 SD 6	89 SD 12	<0.00001	<90%
Systolic blood pressure (mmHg)	119 SD 26	119 SD 25	117 SD 29	0.25	<94 mmHg
Mid-upper arm circumference (cm)	26.6 SD 4.3	26.7 SD 4.3	25.8 SD 4.3	0.009	<24 cm

bpm, beaths or breaths per minute; cm, centimetre; mmHg, millimetre of mercury.

Discussion

Main findings

This natural experiment found that 8.2% of patients received supplemental oxygen on admission to hospital, and these patients were more than 10 times likely to die than those not given oxygen. The 83% of the patients with oxygen levels below 95%, albeit measured after a delay of up to 16h, who were not given oxygen were nearly 8 times less likely to die. Although the intuitive decision to provide oxygen was not guided by oximetry, it did accurately predict in-hospital mortality: a logistic regression model based on those variables that predicted the use of supplemental oxygen also predicted in-hospital mortality.

Strengths and weaknesses

The major flaw of this observational study is that we cannot tell how many patients on oxygen with oxygen saturations above the 90% or

Table 3 – Odds ratio for being given supplemental oxygen for each of the 20 variables collected.

No.	Variable	Total	*(%)*	Oxygen given	Odds ratio	*(95% CI)*		Chi-square	p
1	Breathless at rest	76	*(2.9%)*	56.6%	17.92	*(10.76*	*29.90)*	235.61	<0.0001
2	Not improving	419	*(16.1%)*	26.7%	7.43	*(5.47*	*10.11)*	223.27	<0.0001
3	O2 sat <90%	164	*(6.3%)*	38.4%	9.43	*(6.49*	*13.71)*	206.78	<0.0001
4	Not alert	244	*(9.4%)*	32.4%	7.87	*(5.63*	*11.01)*	204.22	<0.0001
5	Respiratory rate >27 bpm	319	*(12.3%)*	28.5%	7.00	*(5.09*	*9.62)*	195.13	<0.0001
6	Unstable	946	*(36.4%)*	17.2%	6.54	*(4.65*	*9.21)*	157.46	<0.0001
7	Heart rate >114 bpm	205	*(7.9%)*	28.3%	5.66	*(3.94*	*8.13)*	115.65	<0.0001
8	Feels weak	1857	*(71.5%)*	11.3%	18.69	*(7.34*	*52.04)*	77.16	<0.0001
9	Suspected stroke	71	*(2.7%)*	29.6%	5.08	*(2.87*	*8.93)*	41.15	<0.0001
10	Age >64 years	739	*(28.4%)*	13.0%	2.2	*(1.64*	*2.97)*	30.05	<0.0001
11	Medical patient	2047	*(78.8%)*	9.5%	2.95	*(1.78*	*4.95)*	20.50	<0.0001
12	Temperature <36.1 °C	601	*(23.1%)*	12.5%	1.91	*(1.40*	*2.60)*	17.92	<0.0001
13	MUAC <24 cm	590	*(22.7%)*	11.4%	1.62	*(1.18*	*2.23)*	9.32	0.002
14	Systolic blood pressure <94 mmHg	344	*(13.2%)*	11.9%	1.63	*(1.11*	*2.38)*	6.57	0.01
15	Female gender	1285	*(49.4%)*	9.6%	1.42	*(1.06*	*1.91)*	5.68	0.02
16	Known to be HIV negative	1925	*(74.1%)*	7.5%	0.71	*(0.52*	*0.98)*	4.48	0.03
17	Actively vomiting	210	*(8.1%)*	4.8%	0.54	*(0.26*	*1.06)*	3.16	0.08
18	In pain	1353	*(52.1%)*	7.4%	0.79	*(0.59*	*1.06)*	2.43	0.12
19	Current diarrhoea	111	*(4.3%)*	7.2%	0.86	*(0.38*	*1.87)*	0.05	0.82
20	Actively bleeding	44	*(1.7%)*	6.8%	0.81	*(0.20*	*2.79)*	0.00	0.95

O2sat, oxygen saturation; bpm, beats or breaths per minute; MUAC, mid-upper arm circumference; mmHg, millimetre of mercury

Table 4 – Nine variables that were significantly associated with the provision of supplementary oxygen after adjustment by logistic regression. A simple predictive model was the sum of all the coefficients to the nearest integer.

Variable	Odd ratio	*(95% CI)*		Coefficient	SE	Score points
Feeling weak	8.17	*(3.25*	*20.5)*	2.1	0.47	2
Breathless at rest	6.63	*(3.73*	*11.79)*	1.89	0.29	2
Oxygen saturation <90%	4.05	*(2.61*	*6.28)*	1.4	0.22	1
Not alert	3.66	*(2.44*	*5.48)*	1.3	0.21	1
Heart rate >114 bpm	3.21	*(2.07*	*4.99)*	1.17	0.22	1
Respiratory rate >27 bpm	3.15	*(2.16*	*4.6)*	1.15	0.19	1
Unstable gait	2.36	*(1.59*	*3.5)*	0.86	0.2	1
Temperature <36.1 °C	2.31	*(1.6*	*3.33)*	0.84	0.19	1
Medical admission	2.06	*(1.2*	*3.53)*	0.72	0.28	1

Hosmer−Lemshow goodness of fit statistic p = 0.49.
bpm, beats or breaths per minute.

95% had lower levels before oxygen was started. Data were only entered after the patient was admitted to the hospital, and there may have been a delay of up to 16 h between admission to the ward and data collection. Therefore, it is entirely possible that oxygen saturation in the emergency department, had it been measured, would have been significantly different, and altered by subsequent treatment.

This study was performed in a single centre, was relatively small, and only examined in-hospital mortality as no follow-up was possible after discharge. Therefore, the number of patients who may have died shortly after discharge is unknown. The study only included patients who survived to admission and, therefore, did not include moribund patients who died within minutes of arrival at the hospital.

The only candidate variables that could be examined were those collected by the hospital's current routine assessment made every time vital signs are measured, which contained subjective assessments that may have been prone to bias. Some symptoms and signs not found to be associated with mortality in the past, such as rigors, were not included.[21] It is possible that other factors that were not collected may also have predicted supplemental oxygen use. We were not able to determine, for example, how many patients who needed oxygen refused it or could not afford to pay for it.

Interpretation

The purpose of this study was to identify the factors that might influence the use of supplemental oxygen, and not to develop or validate a robust predictive score for either oxygen use or in-hospital mortality. The nine variables of the final predictive model have all already been reported to be associated with mortality: in most hospitals medical patients are more likely to die than surgical patients, apart from those with major trauma[22]; several studies have demonstrated in-hospital death's association with shortness of breath at rest and a sense of weakness,[23,24] abnormal vital signs,[25] altered mental status[26] and impaired mobility.[27] The data examined reflected

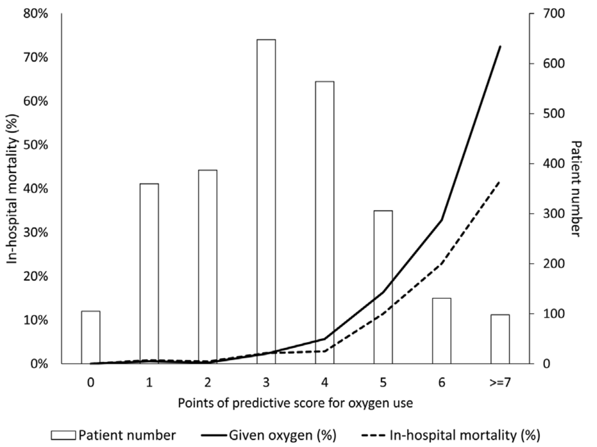

Fig. 2 – Proportion of patients given supplemental oxygen and in-hospital mortality according to the logistic regression model for the prediction of supplemental oxygen use.

the patients' condition at the time it was collected. In a different cohort of patients 16.3% complained of weakness and 8.6% of breathlessness as a reason for admission, yet neither symptom was associated with an increased risk of mortality.[28] In contrast in this cohort 3% of patient were breathless at rest at the time of they were assessed and were six times more likely to die, while 70% complained of weakness when assessed and were eight times more likely to die. This study also confirms our previous report that patients who feel they were improving have a better outcome.[29] Others have also reported a similar correlation between patients' subjective feelings and severity of illness.[30]

Clinical relevance

Regardless of their oxygen saturation, this study found that patients given supplemental oxygen had a significantly higher mortality than those not given it. As this difference in mortality was large it is unlikely that any potential damage from oxygen[9] could account for it. The most plausible explanation is that patients given oxygen were either consciously or unconsciously recognized as being sicker than those not given it. Guidelines disagree on the saturation level below which supplemental oxygen should be given, ranging from 90% to 95%.[4,6,8,31] If an oxygen saturation of <95% had been used as an indication for oxygen use, nearly 30% of patients would have required it. Very few, if any, low-resource hospitals, or their patients would be able to afford to do this.[14] Without clear evidence of benefit from oxygen therapy for patients with oxygen saturations between 90% and 94%, a practical recommendation for oxygen therapy in low resource settings would be to provide it for all patients with oxygen saturations below 90%. Had this recommendation been followed oxygen supplementation would have been indicated in only 6.3% of our patients, which is less than the 8.2% who were given it in this study.

Whilst world-wide oxygen is probably the most used drug in medical emergencies,[4,6] this is not the case in low-resource settings. Since the availability of oxygen is limited and expensive the decision to provide it is a conscious and deliberate one, and usually would require the consent of the patient or their relatives. Our results suggest that this joint decision is influenced by the patient's distress, the apparent severity of their condition and their perceived impending risk of demise. In many parts of sub-Saharan Africa oximetry is not freely available and, as our results suggest, its value often not appreciated or understood. In the past it has been suggested that oximetry is unaffordable in low resource settings,[32] but this is no longer true: cheap (∼US$30) accurate and robust pulse oximeters are now widely available.

The decision to give oxygen to the patients in this study was probably a rapid one based on the combined intuition of inexperienced clinicians and/or patients and/or their relatives, which accurately discriminated between patients who are likely to survive and those who are likely to die at least as well as many explicit scoring systems.[33] Others have also reported that intuition can effectively recognize life-threatening illness.[34–38] In a systematic literature review Douw et al.[39] identified underlying signs and symptoms that intuitively 'worry' nurses. Of these changes in breathing, circulation, mentation, temperature, and the patient's subjective feelings are shared with our findings.

In 1997 the Ethics Committee of the Society of Critical Care Medicine argued against using scoring systems to predict outcome for individual patients,[40] which implied that intuition should be used as an alternative. However, intuition is a feeling and not a thought than can be analysed and understood. It may not distinguish patients with potentially reversible life-threatening illness from those who are "actively dying"[41] and require palliative care. Furthermore, it may not trigger appropriate interventions are efficiently as predictive scores. If intuition alone is used to make decisions such as the withdrawal of care, then there is a risk its predictions will be self-fulfilling. If patients in this study were given oxygen as palliation because it was thought they were "actively dying", then in two thirds of cases this intuition was wrong as most patients given oxygen survived at least until hospital discharge. Sick people and dying people often look the same, and a fall in oxygen saturation frequently occurs in patients who are "actively dying".[42] Although there are clinical features that are thought to identify "actively dying" patients, such as drooping nasolabial folds,[43] these have not been adequately researched or validated.

Conclusion

In a low-resource hospital in sub-Saharan Africa the intuitive decision to provide supplemental oxygen made without the aid of oximetry was strongly associated with in-hospital mortality. The trained use of oximetry might guide oxygen therapy more efficiently.

Funding and conflict of interest statement

All costs were borne by the authors. John Kellett is a major shareholder, director, and chief medical officer of Tapa Healthcare DAC. The other authors have no potential conflicts of interest.

Authors' contributions

All authors contributed to the preparation of this paper. LW-K, PN and JK conceived the study; LW-K and PN supervised the collection of the data; IN, JN and TN collected the data and made practical suggestions to ensure its accuracy, JK analysed the data; LW-K, PN and JK drafted the manuscript and critically revised the manuscript for intellectual content. All authors read and approved the final manuscript and are guarantors of the paper.

Ethical approval

Ethical approval of the study was obtained from the Scientific Ethics Committee Kitovu Hospital, which conformed to the principles outlined in the Declaration of Helsinki. Since no interventions were additional to the usual standard of care the need for written consent was waived.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.resplu.2020.100056.

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