

Electrolyte and Metabolic Disturbances in Ebola Patients during a Clinical Trial, Guinea, 2015

Johan van Griensven, Elhadj Ibrahima Bah, Nyankoye Haba, Alexandre Delamou, Bienvenu Salim Camara, Kadio Jean-Jacques Olivier, Hilde De Clerck, Helena Nordenstedt, Malcolm G. Semple, Michel Van Herp, Jozefien Buyze, Maaïke De Crop, Steven Van Den Broucke, Lutgarde Lynen, Anja De Weggheleire, the Ebola-Tx Consortium

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Learning Objectives

Upon completion of this activity, participants will be able to:

- Distinguish laboratory abnormalities among patients with Ebola virus disease
- Assess risk factors for mortality among patients with Ebola virus disease
- Determine the risk stratification for mortality outcomes with Ebola virus disease
- Analyze the management of laboratory abnormalities associated with Ebola virus disease

CME Editor

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CME Author

Charles P. Vega, MD, Clinical Professor of Family Medicine, University of California, Irvine. *Disclosure: Charles P. Vega, MD, has disclosed the following financial relationships: served as an advisor or consultant for Allergan, Inc.; McNeil Consumer Healthcare; served as a speaker or a member of a speakers bureau for Shire Pharmaceuticals.*

Authors

Disclosures: Johan van Griensven, PhD; Elhadj Ibrahima Bah, MD; Nyankoye Haba, MSc; Alexandre Delamou, MD; Bienvenu Salim Camara, MD; Kadio Jean-Jacques Olivier, PharmD, MPH; Hilde De Clerck, MD; Malcolm G. Semple, MD, PhD; Michel Van Herp, MD; Jozefien Buyze, PhD; Maaïke De Crop, MSc; Steven Van Den Broucke, MD; Lutgarde Lynen, PhD; and Anja De Weggheleire, MD, MPH, have disclosed no relevant financial relationships. Helena Nordenstedt, MD, PhD, has disclosed the following relevant financial relationship: employed by a commercial interest (partner employed): Gilead.

Author affiliations: Institute of Tropical Medicine, Antwerp, Belgium (J. van Griensven, J. Buyze, M. De Crop, S. Van Den Broucke, L. Lynen, A. De Weggheleire); Donka National Hospital, Conakry, Guinea (E.I. Bah); National Blood Transfusion Center, Conakry (N. Haba, B.S. Camara, K.J.-J. Olivier); National Center for Training and Research

in Rural Health of Maferinyah, Forecariah, Guinea (A. Delamou); Médecins Sans Frontières, Brussels, Belgium (H. De Clerck, H. Nordenstedt, M. Van Herp); University of Liverpool, Liverpool, United Kingdom (M.G. Semple)

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By using data from a 2015 clinical trial on Ebola convalescent-phase plasma in Guinea, we assessed the prevalence of electrolyte and metabolic abnormalities at admission and their predictive value to stratify patients into risk groups. Patients underwent testing with a point-of-care device. We used logistic regression to construct a prognostic model and summarized the predictive value with the area under the receiver operating curve. Abnormalities were common among patients, particularly hypokalemia, hypocalcemia, hyponatremia, raised creatinine, high anion gap, and anemia. Besides age and PCR cycle threshold value, renal dysfunction, low calcium levels, and low hemoglobin levels were independently associated with increased risk for death. A prognostic model using all 5 factors was highly discriminatory (area under the receiver operating curve 0.95; 95% CI 0.90–0.99) and enabled the definition of risk criteria to guide targeted care. Most patients had a very low (<5%) or very high (>80%) risk for death.

During the 2014–2016 Ebola virus disease (EVD) outbreak in West Africa, a total of 28,646 cases were diagnosed, with a case-fatality rate of 39.4% (1). Several research groups have focused on new therapeutic interventions, but none has been found to be very effective (2–4). Others have emphasized the importance of good supportive care (5–11). Besides indicating appropriate oral and intravenous hydration, a body of research has also made the case for increasing access to point-of-care (POC) devices to detect metabolic and electrolyte abnormalities (5–8,10–13) because pronounced abnormalities have been observed in Ebola virus patients treated in the United States and Europe (14).

However, the evidence base for this recommendation in busy, resource-limited Ebola treatment units (ETUs) remains limited. If few readily treatable electrolyte disturbances would be detected with these devices, their added value could be questioned because each blood collection puts healthcare workers at risk for infection (15). The limited understanding of the prognostic importance of these abnormalities further obscures the evidence base on their clinical value in resource-constrained settings. Moreover, findings might differ within and between countries, and information from various settings is thus required to inform management guidelines. Despite the ≈30,000 EVD cases diagnosed worldwide over the past 40 years, the evidence base on the prevalence and prognostic value of blood abnormalities is limited to a small number of reports on a fraction of all treated Ebola patients (4,16,17), many of whom were being treated intensively in high-resource settings (14,18,19).

A better understanding of abnormal blood test results could have important clinical consequences. First, more precise information on the prevalence of abnormalities could enable rational decision-making on which testing

to prioritize and which abnormalities treatment programs should prepare to appropriately manage. Identified abnormalities could lead to relevant, simple therapeutic interventions (e.g., potassium [K⁺] supplementation) that could reduce case-fatality rates. Second, identification of factors independently associated with an increased risk for death could lead to better prognostic classification of patients, identifying those in need of higher levels of care, and improve standardization when analyzing results of future clinical trials. To enable clinical decision-making, estimates of the absolute risk for death would be required for individual patients across the spectrum of independent risk factor values (20) and not the mere reporting of group odds or risk ratios, as has been done before (16,17). Based on the predicted absolute risk for death, individual risk stratification could be done on admission.

The Ebola-Tx trial evaluated convalescent-phase plasma as an EVD treatment in a Médecins sans Frontières (MSF) ETU in Conakry, Guinea. Trial findings have been published (2). MSF introduced a POC device during the trial. We used the opportunity of having access to relatively high-quality data from this clinical trial to 1) describe the prevalence of electrolyte and metabolic disturbances during admission and the association with EVD death and 2) assess the predictive value of these prognostic factors to stratify patients in risk groups.

Methods

Ebola-Tx Trial

The Ebola-Tx trial was conducted at the Conakry ETU supported by MSF. Trial patients were recruited during February 17–July 7, 2015. Patients of all ages, including pregnant women, were eligible, and their outcomes were compared with historical controls treated at the same center before the trial began. As per World Health Organization recommendations, patients received 2 units of 200–250 mL of Ebola convalescent-phase plasma after EVD diagnosis was confirmed by PCR (2). For children, a total volume of 10 mL/kg of Ebola convalescent-phase plasma was given. The level of neutralizing antibodies in the donors was unknown at the time of administration. Although the trial was found safe and feasible to organize, the efficacy of convalescent-phase plasma was not proven; the adjusted absolute risk reduction was -3% (95% CI -13% to 8%) (2).

Supportive Care at the MSF ETU

Supportive care during the trial was provided by the MSF team as per MSF guidelines. As part of supportive care, MSF staff introduced a POC device (i-STAT; Abbott Point of Care, Princeton, NJ, USA) on February 25, 2015, soon after the trial began. All patients were tested at the time of EVD diagnosis by using CHEM8+ cartridges (Abbott

Point of Care) to determine levels of electrolytes (K^+ , sodium [Na^+], chloride [Cl^-], and ionized calcium [iCa^{2+}]), creatinine, and blood urea nitrogen (BUN); the anion gap; the total amount of dissolved carbon dioxide (TCO_2); glucose levels; and hemoglobin/hematocrit values.

The MSF supportive care guidelines recommend empirical systematic prescription of antibiotics and antimalarial drugs. Symptomatic care (e.g., for pain or nausea/vomiting) was given as needed. Fluid replenishment was done with oral rehydration fluids if a patient was alert, not vomiting, and able to participate in their own care. Intravenous fluids were given to patients with insufficient oral intake, severe vomiting or diarrhea, pronounced or persistent hypotension, or clinical signs of severe dehydration (21).

Study Population

A total of 102 patients were enrolled in the Ebola-Tx trial, of whom 98 received convalescent-phase plasma. A total of 87 were recruited after the introduction of the POC device.

Data Collection

During the trial, data were entered in an electronic case report form directly from source documents, which, when filled in the high-risk zone, were scanned using mobile phones and transmitted over a secured local wireless network to a central server and automated printer. Data were collected on admission and each day after EVD confirmation, including information on symptoms and clinical signs of EVD, vital signs, and treatment received. For our study, we used all available data on the POC results on admission, cycle threshold (C_t) values of the Ebola diagnostic PCR, baseline patient characteristics, and discharge status.

Definitions

We used definitions based on the POC device normal values and standard definitions for abnormalities: hypokalemia, $K^+ < 3.5$ mmol/L; moderate hypokalemia, $K^+ 2.5$ – 3.0 mmol/L; severe hypokalemia, $K^+ < 2.5$ mmol/L; hyperkalemia, $K^+ \geq 5.0$ mmol/L; hyponatremia, $Na^+ < 135$ mmol/L; hypernatremia, $Na^+ > 146$ mmol/L; hypochloremia, $Cl^- < 98$; high anion gap, > 20 ; low TCO_2 , < 24 mmol/L; low glucose, < 70 mg/dL; high glucose > 180 mg/dL; creatinine and BUN: mild increase, 1.0–1.5 times the upper limit of normal (ULN); moderate increase, 1.5–3.0 times ULN; severe, > 3.0 times ULN; increased BUN/creatinine ratio, > 20 ; and hypocalcemia, $iCa^{2+} < 1.12$ mmol/L. Anemia was defined per World Health Organization guidelines (age/sex adjusted) using hemoglobin values (22).

Statistical Analysis

We calculated medians and interquartile ranges (IQRs) for continuous variables and summarized binary/categorical data by using frequencies and percentages. We compared groups

by using Fisher exact tests for binary/categorical variables and the Wilcoxon rank-sum test for continuous variables.

The outcome status at the time of discharge from the MSF ETU was classified as alive or dead, excluding patients transferred to another ETU. We performed a risk factor analysis by using multivariate logistic regression modeling to determine independent factors associated with increased risk for death. We selected a restricted number of exposure variables on the basis of theoretical considerations and published studies. We included the following variables in the POC model: K^+ , iCa^{2+} , and creatinine levels; anion gap; amount of TCO_2 ; glucose levels; and hemoglobin levels. The POC+ model included the same POC variables plus age and the C_t of the PCR at EVD diagnosis, given that these 2 additional variables are the most universally accepted prognostic factors (4,23,24). To maximize power, we included the variables as continuous variables and determined the functional form by using the fracpoly command (fractional polynomial regression, which fits fractional polynomials as part of the specific regression model) in Stata version 14 (StataCorp LP, College Station, TX, USA). We reduced the model by using backward stepwise elimination until all variables had a p value < 0.05 . By using the logistic regression coefficients from the final model, we calculated the predicted risk for death for each patient and plotted the results in a histogram. We summarized the predictive value of the model by calculating the area under the receiver operating curve (AUROC) separately for the POC and the POC+ model.

We tabulated predicted and observed deaths across different predicted risk groups ($< 5.0\%$, 5.0% – 19.9% , 20.0% – 49.9% , 50.0% – 79.9% , and $\geq 80.0\%$). We formally assessed the goodness-of-fit of the model by using the Hosmer-Lemeshow test, yielding a p value < 0.05 , which suggests significant discrepancy between the observed and predictive outcomes. We conducted internal validation by using cross-validation ($h = 10$, $k = 10$) (25). We randomly divided the data into 10 mutually exclusive subsets of the same size. We conducted a 10-fold cross-validation by repeating the analysis 10 times, each time excluding 1 of the independent datasets, and calculating the AUROC. We averaged the summary estimates of the 10 AUROCs to obtain the cross-validation AUROC. We conducted statistical analysis by using Stata version 14.

Results

Of the 87 study patients enrolled in the trial when the POC device was in use, POC results were available for 85 (Table 1). The median age was 30 years (IQR 20–40 years); 48 (56%) patients were female. The median C_t value in the diagnostic PCR was 27 (IQR 18–36).

Hyponatremia (77.6%) was very common, but hypernatremia was only rarely documented (Table 2). Although

Table 1. Baseline characteristics of 85 Ebola patients recruited for the Ebola-Tx trial, Conakry, Guinea, 2015*

Characteristic	Value
Age, median y (IQR)	30 (20–40)
<15	10 (11.8)
Sex	
M	37 (43.5)
F	48 (56.5)
C_t value on diagnostic Ebola PCR, n = 84	
No. cycles, median (range)	26.8 (17.8–35.8)
<25	23 (27.4)
25.0–29.9	40 (47.6)
≥30	21 (25.0)
Duration of symptoms, median d (IQR), n = 74	4 (3–5)
Coexisting chronic medical condition	15 (17.6)
Infectious†	8 (9.4)
Noninfectious‡	7 (8.2)
Selected symptoms on admission	
Nausea and vomiting	43 (50.6)
Diarrhea	29 (34.1)

*Values are no. (%) patients except as indicated. C_t , cycle threshold; IQR, interquartile range.
†For example, tuberculosis, HIV, or malaria.
‡For example, diabetes mellitus, arterial hypertension, chronic cardiac, pulmonary disease, or renal disease.

hypokalemia (33%) was common, severe hypokalemia ($K^+ < 2.5$ mmol/L) and hyperkalemia were rare. Hypocalcemia (64%) was frequently observed. Renal dysfunction (45% with increased creatinine levels), an increased anion gap (28%), and decreased TCO_2 (71%) all were frequently documented. Anemia was observed in 27% of patients.

In the multivariate logistic regression modeling, decreased iCa^+ and hemoglobin levels and increased creatinine levels were associated with increased risk for death (POC model). In the POC+ model, age and the diagnostic PCR C_t value were additionally selected (Table 3). A prediction model based on these 5 factors provided estimates of the risk for death ranging from 0.016% to 99.99%, compared with a baseline (or pretest) risk for death of 34.6% (27/78 patients). The largest risk groups were patients at either very low or very high risk, with 40% of patients having a risk for death <10% and 22% having a risk >80% (Figure 1). This POC+ model had an AUROC of 0.95 (95% CI 0.90–0.99), compared with 0.88 (95% CI 0.78–0.97) for the model that only included creatinine, calcium, and hemoglobin levels (POC model) (Figure 2). AUROC cross-validation values were 0.92 (95% CI 0.85–0.99) for the POC+ model and 0.85 (95% CI 0.75–0.96) for the POC model. The Hosmer-Lemeshow test yielded a p value of 0.98 for the POC+ model and 0.34 for the term POC model. The predicted and observed risk for death was stratified into 5 risk groups (Table 4); most patients were in the <5% or >80% risk group categories.

Discussion

We documented a high prevalence of multiple electrolyte and metabolic abnormalities in Ebola patients at the time of admission during a clinical trial of convalescent-phase

plasma in Guinea. Increased creatinine and decreased calcium and hemoglobin levels during admission were independent risk factors for death. The POC model including these factors and the POC+ model additionally including 2 key risk factors (C_t value of the diagnostic Ebola PCR and the age of the patient) both performed well in predicting individual patient outcome. The predicted risk for death ranged from <0.02% to 99.9%, and most patients were found to have either a very low risk (<5%) or a very high risk (>80%) for death.

The frequent observance of electrolyte disturbances is in line with the few available studies from Africa (17,26). The high prevalence of hypokalemia is of particular interest, although it was rarely severe at the time of admission. Nevertheless, hypokalemia can potentially be fatal and is amenable to relatively simple interventions. A deficiency in iCa^+ was common, a finding also frequently observed in sepsis patients (27,28). In the case of EVD, renal dysfunction and pancreatitis also could contribute. The high anion gap and low TCO_2 are likely explained by lactic acidosis. Renal failure was also common in our study. The exact cause of renal dysfunction in EVD patients remains undefined, but both prerenal and renal causes probably are involved.

The POC+ model, a 5-measure prognostic tool, enabled the stratification of patients into different risk groups at baseline, with risk for death ranging from <5% to >80%. This tool could enable the refining of clinical care pathways and rational use of scarce human resources. Absolute risks for death could easily be calculated via a spreadsheet or smartphone application. Alternatively, scoring systems could be developed for bedside use (29,30).

However, several issues need to be addressed before such prognostic tools are taken forward. First, we did not include other potentially relevant measures that can be tested with POC devices, such as liver function tests, coagulation abnormalities, or markers of inflammation. Although our system performed fairly well with only a few markers, evaluation of the full panel of tests could possibly lead to further improvement. Second, the sample size in our study was limited, and all but 2 of the patients received convalescent-phase plasma. Although transfusion of 500 mL of plasma probably will not strongly influence the prognostic associations, larger studies in different study populations are required to assess the generalizability of our findings. Third, corrective measures for some abnormalities (e.g., hypoglycemia or hypokalemia) could have obscured associations with survival. Moreover, because this was an exploratory study, our findings need to be validated in other and larger datasets. Finally, it remains to be seen whether (and if so how much) our prognostic tool would perform substantially better than clinical judgement alone or a prognostic tool relying on clinical signs/symptoms combined

Table 2. Metabolic and electrolyte disturbances in 85 Ebola patients recruited for the Ebola-Tx trial and association with increased risk for death, Conakry, Guinea, 2015*

Analyte	Value			p value
	Total	Deceased	Survived	
Total†	85	27	51	
K ⁺ , mmol/L median (IQR)	3.7 (3.2–4.2)	3.9 (3–2–4.7)	3.7 (3.2–4.0)	0.21
High	4 (4.7)	3 (11.1)	0 (0)	
Normal	53 (62.3)	16 (59.3)	33 (64.7)	
Mild decrease	12 (14.1)	4 (14.8)	7 (13.7)	0.19
Moderate decrease	14 (16.5)	4 (14.8)	9 (17.6)	
Severe decrease	2 (2.3)	0 (0)	2 (3.9)	
Na ⁺ , mmol/L median (range)	135 (132–137)	132 (129–138)	136 (133–137)	0.055
Low	66 (77.6)	20 (74.1)	39 (76.5)	
Normal	18 (21.2)	6 (22.2)	12 (23.5)	0.52
High	1 (1.2)	1 (3.7)	0 (0)	
Cl ⁻ , mmol/L median (IQR)	99 (95–103)	101 (97–105)	99 (96–102)	0.41
Low	34 (40.0)	10 (37.0)	18 (35.3)	1.0
iCa ²⁺ , mmol/L median (IQR)	4.3 (4.0–4.6)	3.9 (3.5–4.2)	4.4 (4.2–4.7)	<0.01
Low	54 (63.5)	24 (88.9)	26 (51.0)	<0.01
TCO ₂ , mmol/L median (IQR)	21 (18–24)	17 (16–22)	21 (19–25)	<0.01
Low	60 (70.6)	23 (85.2)	37 (72.5)	0.27
Anion gap, mmol/L median (IQR)	19 (17–21)	19 (18–21)	18 (17–20)	0.26
High	24 (28.4)	11 (40.7)	10 (19.6)	0.061
Creatinine, mmol/L median (IQR), n = 84	106 (75–332)	442 (148–654)	91 (63–116)	<0.01
Normal	47 (55.9)	5 (18.5)	38 (74.5)	
1–3x ULN	16 (19.0)	5 (18.5)	9 (17.6)	<0.01
>3x ULN	21 (25.0)	17 (63.0)	4 (7.8)	
BUN, mmol/L median (IQR), n = 84	16 (9–39)	50 (17–69)	11 (7–21)	<0.01
Normal	53 (63.1)	9 (33.3)	38 (76.0)	
1–3x ULN	26 (30.9)	13 (48.1)	12 (24.0)	<0.01
>3x ULN	5 (6.0)	5 (18.5)	0 (0.0)	
BUN/creatinine ratio, median (IQR), n = 83	10.3 (7.4–13.9)	8.8 (6.8–13.9)	11.2 (7.7–14.0)	0.30
<10	36 (43.4)	15 (55.6)	18 (36.0)	
10–20	39 (47.0)	10 (37.0)	26 (52.0)	0.27
>20	8 (9.6)	2 (7.4)	6 (12.0)	
Glucose, mmol/L median (IQR)	121 (104–148)	112 (88–146)	122 (106–147)	0.24
Low	5 (5.9)	4 (14.8)	1 (2.0)	
Normal	72 (84.7)	19 (70.4)	47 (92.2)	0.022
High	8 (9.4)	4 (14.8)	3 (5.9)	
Hemoglobin, g/dL median (IQR)	14.6 (11.9–16)	13.6 (10.5–17)	14.3 (11.9–15.6)	0.90
Anemia‡	23 (27.1)	9 (33.3)	14 (27.4)	0.61

*Values are no. (%) patients except as indicated. BUN, blood urea nitrogen; Cl⁻, chloride; iCa²⁺, ionized (free) calcium; IQR, interquartile range; K⁺, potassium; Na⁺, sodium; TCO₂, total dissolved carbon dioxide; ULN, upper limit of normal value.

†Denominator for deceased and survived patients combined is 78, excluding 7 patients who were transferred to another Ebola treatment unit, where they received favipiravir.

‡Definition of anemia per World Health Organization guideline (age/sex adjusted; hemoglobin levels used).

with age and the PCR C_t value. Nevertheless, a prognostic clinical tool using laboratory measures will have the advantage of being more objective, less variable between clinicians, and less dependent on specific clinical skills.

In contrast to fixed variables such as age and the PCR C_t value that are only useful as prognostic markers, the detection of hypocalcemia, anemia, and renal dysfunction is amenable to interventions. If these conditions are causally associated with an increased risk for death, their detection could contribute to reducing case-fatality rates. If they are only a proxy for another causal factor, correction of these abnormalities might have minimal effects. For instance, surprisingly limited evidence exists that correction of hypocalcemia in intensive care patients improves survival (27), and some evidence suggests that it could even be detrimental (28). Similarly, whether blood transfusion in cases of anemia can improve EVD sur-

vival (and at what threshold hemoglobin value) requires further study. Anemia has been found to be associated with an increased risk for death in other inflammatory conditions such as sepsis (31). However, subsequent studies demonstrated that a liberal blood transfusion strategy could have a negative impact on survival in intensive care patients (32).

The association of renal dysfunction with an increased risk for death has been demonstrated before (4,17,26,33). However, the added clinical value of being able to diagnose renal dysfunction, beyond its prognostic value, in the typical ETU in countries of Africa remains unclear. It could enable staff to more carefully assess the fluid status and thus avoid over- and under-hydration. However, renal dysfunction could be prerenal (requiring aggressive fluid administration) or renal (requiring more cautious fluid administration) in origin. Carefully assessing fluid status in busy ETUs with

Table 3. Factors associated with increased risk for death among 78 Ebola patients recruited for the Ebola-Tx trial, Conakry, Guinea, 2015*

Blood test result†	POC model		POC+ model‡, aOR (95% CI)
	Crude OR (95% CI)	aOR (95% CI)	
K ⁺ , per unit increase	1.7 (0.9–3.3)	–	–
iCa ²⁺ , per 0.1-unit increase)	0.70 (0.59–0.84)	0.78 (0.63–0.96)	0.73 (0.57–0.95)
Glucose, per 50-unit increase)	0.87 (0.50–1.52)	–	–
Creatinine, per 100-unit increase)	2.1 (1.5–3.0)	2.1 (1.3–3.3)	2.3 (1.1–4.6)
TCO ₂ , per 5-unit increase)	0.38 (0.20–0.74)	–	–
Anion gap, per 5-unit increase)	1.5 (0.6–3.7)	–	–
Hemoglobin, per 1-unit increase)	1.0 (0.9–1.2)	0.79 (0.63–0.99)	0.67 (0.47–0.93)
C _t value, per 1-unit increase)	0.80 (0.70–0.93)	–	0.73 (0.56–0.94)
Age, per 10-y increase)	1.8 (1.3–2.6)	–	2.7 (1.2–6.4)

*aOR, adjusted odds ratio; C_t, cycle threshold; iCa²⁺, ionized (free) calcium; K⁺, potassium; OR, odds ratio; POC, point-of-care; TCO₂, total dissolved carbon dioxide.

†No evidence of nonlinearity of the continuous variables except for glucose, which was transformed to the power of –2.

‡POC+ model includes 3 POC measurements (blood creatinine, calcium, and hemoglobin) plus the cycle threshold value of the diagnostic Ebola PCR result and the age of the patient.

brief patient contact remains challenging, and to what extent the ratio of BUN to creatinine is accurate in EVD patients is unclear (17). Whether biochemical diagnosis (and management) of kidney dysfunction substantially improves patient outcomes compared with monitoring urine output and clinically assessing fluid status also remains unknown. It would be more useful to monitor for renal dysfunction if compensatory measures such as dialysis could be put in place (34). Clinical trials would be required to assess this further, looking at case-fatality rate reduction, risk to healthcare staff, and opportunity costs (9). As blood transfusion requires blood group testing and, ideally, bedside cross-matching, risk-benefit assessments for this intervention would also be useful to inform treatment guidelines.

We acknowledge that underestimation of the prevalence of abnormalities is probable because as measurements were not systematically performed during the entire stay in the ETU.

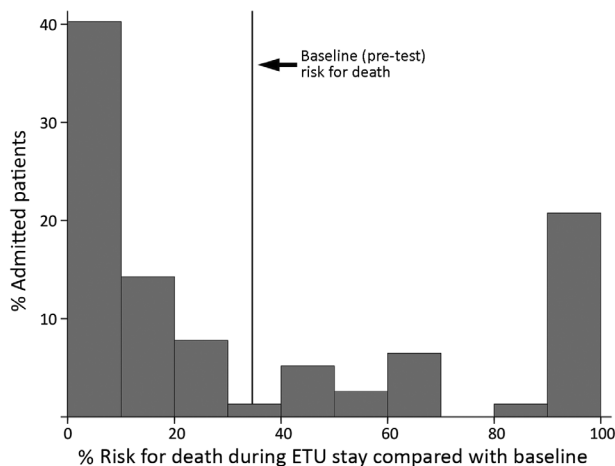


Figure 1. Histogram displaying the distribution of the risk for death for Ebola patients recruited for the Ebola-Tx trial, Conakry, Guinea, 2015, according to a 5-variable point-of-care (POC+) prognostic prediction model. POC+ model includes 3 POC measurements (blood creatinine, calcium, and hemoglobin) plus the cycle threshold value of the diagnostic Ebola PCR result and the age of the patient. ETU, Ebola treatment unit.

Still, our findings show that a POC device is practical to use in the ETU and could be useful in stratifying patients into risk groups at baseline. Information on the extent POC results were used by the clinicians would also have strengthened the study.

In conclusion, in the challenging environment of an ETU, staff wearing full protective equipment were able to use a POC device that frequently detected metabolic and electrolyte abnormalities among EVD patients at admission. Besides age and diagnostic PCR C_t value, renal dysfunction, low calcium levels, and low hemoglobin levels were independently associated with an increased risk for death. A clinical prognostic model using these 5 factors had a high discriminatory potential, with most patients having either very low (<5%) or very high (>80%) risk for death. To what extent interventions aiming at correcting the observed abnormalities can reduce case-fatality rates remains to

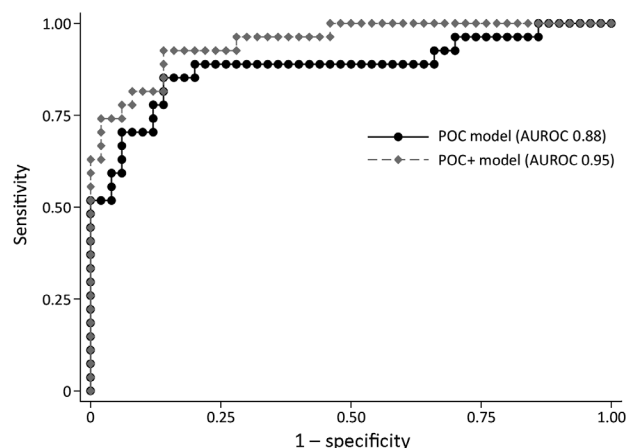


Figure 2. Receiving operating curve summarizing the performance of 3-variable point-of-care (POC) and 5-variable POC+ prognostic prediction models for Ebola patients recruited for the Ebola-Tx trial, Conakry, Guinea, 2015. POC model includes blood creatinine, hemoglobin, and calcium levels. POC+ model includes the same 3 POC measurements plus the cycle threshold value of the diagnostic Ebola PCR result and the age of the patient. AUROC, area under the receiver operating curve; POC, point-of-care.

Table 4. Predicted and observed deaths across risk categories among 77 Ebola patients recruited for the Ebola-Tx trial, according to the POC+ model, Conakry, Guinea, 2015*†

Death risk category (predicted), %	Total no. patients (column %)	No. deaths observed (row %)	No. deaths predicted (row %)
0–4.9	28 (36.4)	1 (3.6)	0.4 (1.5)
5.0–19.9	14 (18.2)	1 (7.1)	1.7 (12.3)
20.0–49.9	11 (14.3)	4 (36.4)	3.7 (34.0)
50.0–79.9	7 (9.1)	4 (57.1)	4.4 (63.5%)
80.0–100	17 (22.1)	17 (100.0)	16.7 (98.1)

*One recruited patient was excluded because of a missing C_t value. C_t , cycle threshold; POC, point-of-care.

†POC+ model includes 3 POC measurements (blood creatinine, calcium, and hemoglobin) plus the cycle threshold value of the diagnostic Ebola PCR result and the age of the patient.

be assessed. Moreover, risk-benefit assessments that consider the risks to healthcare workers are required to inform treatment guidelines.

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Dr. van Griensven acted as coordinating investigator of the Ebola-Tx trial and is currently leading the unit of HIV and Neglected Tropical Diseases at the Institute of Tropical Medicine in Antwerp, Belgium. His primary research interests include leishmaniasis and emerging infectious disease outbreaks.

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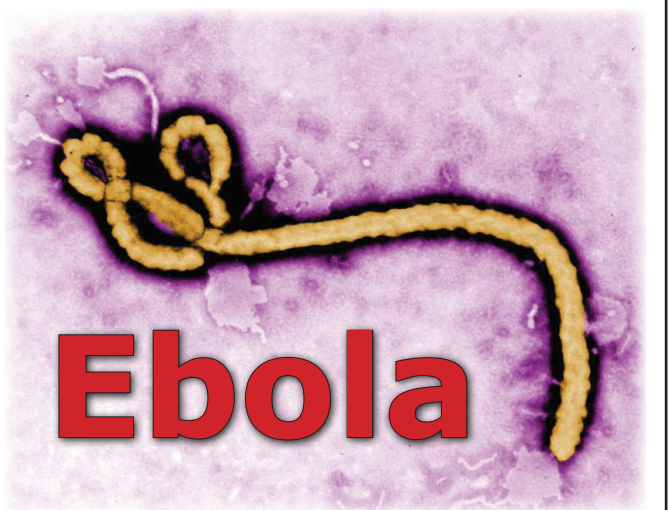
Address for correspondence: Johan van Griensven, Nationalestraat 155, 2000 Antwerp, Belgium; email: jvangriensven@itg.be

EID SPOTLIGHT TOPIC

Ebola, previously known as Ebola hemorrhagic fever, is a rare and deadly disease caused by infection with one of the Ebola virus strains. Ebola can cause disease in humans and nonhuman primates (monkeys, gorillas, and chimpanzees).

Ebola is caused by infection with a virus of the family *Filoviridae*, genus *Ebolavirus*. There are five identified Ebola virus species, four of which are known to cause disease in humans. Ebola viruses are found in several African countries; they were first discovered in 1976 near the Ebola River in what is now the Democratic Republic of the Congo. Before the current outbreak, Ebola had appeared sporadically in Africa.

The natural reservoir host of Ebola virus remains unknown. However, on the basis of evidence and the nature of similar viruses, researchers believe that the virus is animal-borne and that bats are the most likely reservoir. Four of the five virus strains occur in an animal host native to Africa.



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