IDENTIFYING RESOURCE NEEDS FOR SEPSIS CARE AND GUIDELINE IMPLEMENTATION IN THE DEMOCRATIC REPUBLIC OF THE CONGO: A CLUSTER SURVEY OF 66 HOSPITALS IN FOUR EASTERN PROVINCES

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Abstract

The ongoing conflict in the Eastern Republic of the Congo (DRC) has claimed up to 5.4 million lives by 2008. Whereas few deaths were directly due to violence, most victims died from medical conditions such as infectious diseases. This survey investigates the availability of resources required to provide adequate sepsis care in Eastern DRC.

The study was conducted as a self-reported, questionnaire-based survey in four Eastern provinces of the DRC. Questionnaires were sent to a cluster of 80 urban-based hospitals in the North Kivu, South Kivu, Maniema and Orientale provinces. The questionnaire contained 74 questions on the availability of resources required to adequately treat sepsis patients as suggested by the latest Surviving Sepsis Campaign (SSC) guidelines.

Sixty-six questionnaires were returned (82.5%) and analyzed. Crystalloid solutions and intravenous fluid giving sets were the only resources constantly available in all hospitals. None of the respondents reported to have constant access to piperacillin, carbapenems, fresh frozen plasma, platelets, dobutamine, activated protein C, echocardiography or equipment to measure lactate levels, invasive blood pressure, central venous pressure, cardiac output, pulmonary artery pressure or endtidal carbon dioxide. No respondent stated that a mechanical ventilator, syringe pump, fluid infuser, peritoneal dialysis or haemodialysis/hemofiltration machine was constantly available at his/her hospital. Resources required for consistent implementation of the SSC guidelines were not available in any hospital.

This survey indicates a critical shortage of resources required to provide adequate sepsis

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care and implement the SSC guidelines in a cluster of hospitals in the Eastern DRC.

Key words: Sepsis; Resources; Surviving Sepsis Campaign Guidelines; Democratic Republic of the Congo; Africa.

Introduction

Over 75% of the global burden of infectious diseases, as assessed by mortality and disability adjusted life years lost, occurs in low-income countries[1,2]. Infectious diseases make up six of the ten most frequent causes of death in these parts of the world[3]. Except for chronic viral diseases such as HIV/AIDS, development of sepsis, organ dysfunction and shock is the common sequence leading to death from infection, irrespective of its underlying focus[4]. Case fatalities of up to 70-100% are observed once infection has led to organ dysfunction or shock in resource-poor environments[5-11]. Accordingly, it must be assumed that severe sepsis and septic shock substantially contribute to the overall mortality of infectious diseases in low-income countries.

The Democratic Republic of the Congo (DRC), known as Zaire until 1997, is home to ~70 million people and ranks among the poorest countries in Sub-Sahara Africa. The DRC's crude mortality rate is the highest in the world[12]. Eastern DRC consists of five provinces (South and North Kivu, Orientale, Maniema, Katanga) and, since 1998, has been torn by an ongoing military conflict characterized by extreme violence, mass population displacements and a collapse of public health services[12]. In a series of mortality surveys, the International Rescue Committee estimated that the war and humanitarian crisis had claimed up to 5.4 million lives by 2008[13]. Whereas <1% of excess deaths were directly due to violence, the vast part of conflict-claimed victims died from preventable and treatable medical conditions with the majority of deaths caused by infectious diseases[14]. Although mortality rates of severe sepsis and septic shock patients are not available for the Eastern DRC, critically ill sepsis patients presenting to two hospitals in neighboring Uganda had mortality rates >50%[10]. A retrospective study from Tunisia reported a fatality rate of 82% for septic shock patients[6], and Kalayi[11] found that no burn patient developing septic shock survived in a Nigerian university teaching hospital.

Although early recognition and timely treatment of infection is crucial in preventing progression to sepsis and organ dysfunction, adequate treatment of severe sepsis and septic shock may additionally save a considerable number of lives. For example, implementation of the Surviving Sepsis Campaign (SSC) guidelines, which summarize the latest clinical evidence in sepsis care[15], improves sepsis care and patient outcome[16-18]. However, implementation of these guidelines requires specific resources which may only be inconsistently available or entirely lacking in Sub-Sahara Africa[19-22]. Detailed data on the availability of resources to treat sepsis could help to identify possibilities to improve sepsis care in the region.

Therefore, this survey investigates the availability of hospital facilities and resources required to provide adequate sepsis care, as suggested by the latest SSC guidelines[15], among hospitals in four Eastern provinces of the DRC. We hypothesized that hospital facilities and resources needed to implement the SSC guidelines were only inconsistently available.

Materials and Methods

This study was conducted as a self-reported, questionnaire-based cluster survey in four Eastern provinces of the DRC. The study protocol and survey instrument were reviewed and approved by the Ethical Committee of the Medical University of Goma/DRC.

In October 2009, 80 questionnaires were sent *via* the postal service from Goma, the capital city of the North Kivu province, to urban-based hospitals in the provinces of North Kivu (n=35), South Kivu (n=12), Maniema (n=13) and Orientale (n=20). Hospitals located in regions with ongoing civil war activities were inaccessible because of security issues or non-existent postal services, and had to be excluded from the sampling frame. Questionnaires were directed either to the health care provider in charge of the intensive care unit or the one responsible for the care of acutely and critically ill patients in the respective hospital if the hospital did not run an intensive care unit. All participants were notified that participation was voluntary and based on the understanding that results would be published in a scientific journal. No

incentives to complete the questionnaire were offered. After two months, health care providers who had so far not responded were contacted and asked to participate. Returned questionnaires were collected at the DOCS Hospital in Goma until February 2010 and then taken to the study centre in Europe for statistical analysis.

The SSC Guidelines

In 2001, 2004 and 2008, international experts released guidelines for the management of severe sepsis and septic shock[15,23-24]. These SSC guidelines are one of the first international consensus guidelines on treatment in intensive care medicine and include initial resuscitation, infection control, hemodynamic support, adjunctive therapy and other supportive therapies for severe sepsis and septic shock patients. In its latest publication (15), the SSC graded their proposals as recommendations and suggestions. Recommendations imply that an intervention's desirable effects clearly outweigh its risks and should be followed by physicians in most situations. Suggestions mean that the relation between desirable and undesirable effects of an intervention is less clear and physicians may consider its use. Furthermore, the SSC assessed the level of clinical evidence for each recommendation and suggestion. Accordingly, recommendations are graded as level I evidence subcategorized from A to D (with A being the highest and D the lowest grade of evidence). Suggestions are uniformly graded as level II evidence.

Questionnaire

The questionnaire used as the survey instrument in this study was designed and based on the latest SSC guidelines[15]. The questionnaire contained 74 questions grouped into seven main categories (general information on the hospital, hospital facilities, drugs, patient monitoring, laboratory, equipment and disposables). Responses were classified as 'yes', 'no', 'don't know' for the category 'hospital facilities' and 'always', 'sometimes', 'never', 'don't know' for the remaining categories. The study questionnaire was translated into the French. The original study questionnaire in English (Electronic Supplementary Material Figure 1) underwent pre-and pilot-testing for ease of completion and inter-observer variability by anaesthetists in Kenya and Tanzania. It has also been used in a cross-sectional survey to evaluate resource availability to implement the SSC guidelines on the African continent and in Mongolia[25].

Outcome Variables

The main outcome variable was availability of resources necessary to provide adequate sepsis care and implement the latest SSC guidelines. Prior to the survey, hospital facilities, equipment, drugs and disposable materials required to implement single SSC recommendations and suggestions were defined by consensus of the study investigators (Electronic Supplementary Material Table 1). For consistent implementation of the SSC guidelines, resources had to be 'always' available. Resources 'sometimes' or 'never' available, as well as those respondents did not know whether resources were available at their hospital were considered insufficient to provide adequate sepsis care and implement the SSC guidelines. Furthermore, the percentage of implementable recommendations and suggestions of the SSC guidelines was calculated for each returned questionnaire.

Table 1
Characteristics of Respondents and Hospitals

n		66
Specialty of Respondent	*n (%)*	31 (47)
Non-Physician Anaesthetist		31 (47)
Nurse Anaesthetist		4 (6.1)
Other		
Type of Hospital	*n (%)*	
District		44 (68.6)
Regional/Provincial		9 (13.6)
University Teaching		2 (3)
Other		11 (16.6)
Size of Hospital	*(beds)*	84 (43-118)
Availability of Hospital Facilities	*n (%)*	
Emergency Room (n=64)		20 (31.3)
Operation Theatre (n=64)		63 (98.4)
Intensive Care Unit (n=64)		27 (42.2)

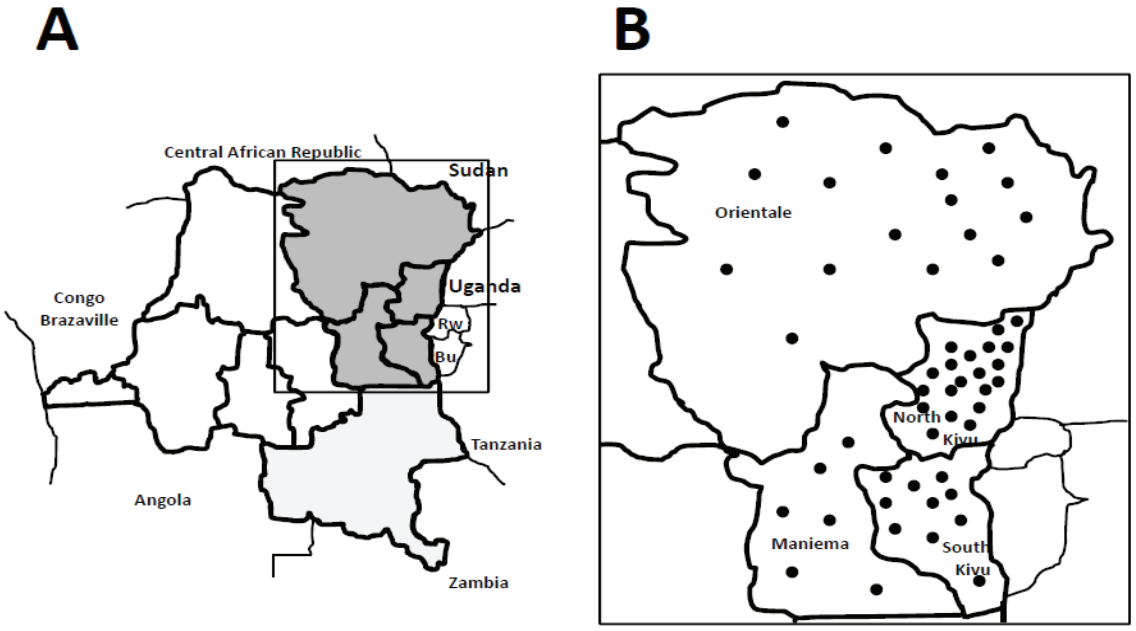
Data are given as median values with interquartile ranges, if not otherwise indicated.

Statistical analysis

Questionnaires were manually entered into a centralized database. After double checking, the database was re-checked by calculating minimum and maximum values of each question to recognize and

Fig. 1

Map of the Democratic Republic of the Congo with the four Eastern provinces surveyed highlighted in grey (A) and the town of responding hospitals in these provinces marked with black dots (B). Please note that some hospitals were located in the same town thus rendering a lower number of dots than responding hospitals.



eliminate remaining entry errors. The SPSS software package (SPSS 13.0.1; SPSS Inc., Chicago, Illinois, United States) was used for statistical analysis. Simple frequencies based on the number of completed questions (some questions were not completed by all respondents) were calculated for all categorical data. Continuous variables are presented as median values with interquartile ranges (IQR).

Results

Of the 80 questionnaires distributed, 66 were returned (82.5%) and statistically analyzed (Figure 1). Seventeen questionnaires (25.8%) were only partially completed. The median number of missing responses in these questionnaires was 3 (IQR, 1-11). Table 1 summarizes characteristics of the survey respondents and their hospitals. Tables 2, 3 and 4 display the availability of drugs, equipment and disposable materials to provide adequate sepsis care and implement the SSC guidelines. Crystalloid solutions and intravenous fluid giving sets were the only resources constantly available in all responding hospitals. None of the respondents reported to have constant access to piperacillin, carbapenems, fresh frozen plasma, platelets, dobutamine, activated protein C, echocardiography or equipment to measure lactate levels, invasive blood pressure, central venous pressure, cardiac output, pulmonary artery pressure or endtidal carbon dioxide at his/her hospital. No respondent stated that a mechanical ventilator, syringe pump, fluid infuser, peritoneal dialysis or haemodialysis/ hemofiltration machine was constantly available at his/her hospital. Resources required for consistent implementation of all SSC recommendations/ suggestions were not available in any hospital (Table 5).

Discussion

This cluster survey included 66 hospitals located in North and South Kivu, Orientale and Maniema provinces and covered large parts of the Eastern DRC (Figure 1). Out of an estimated total of 250 hospitals, a cluster of 80 urban-based hospitals could be studied. Logistic and security issues prevented us from capturing the remaining health care facilities which are mostly located in rural areas. Therefore, our study results can only reflect the current status on resource availability for sepsis care in a selected group of urban-based hospitals. Although these hospitals may be privileged by their location and enhanced security state compared

Table 2. Availability of Drugs to Provide Adequate Sepsis Care and Implement the Surviving Sepsis Campaign Guidelines

		Always	*Sometimes*	*Never*	*Don't Know*
Oxygen (*n* =65)		23 (35.4)	16 (24.2)	26 (39.4)	0
Antibiotics					
	Ampicillin	65 (98.5)	1 (1.5)	0	0
	Gentamycin	45 (68.2)	21 (31.8)	0	0
3rd /4th	*Gen Cephalosporin*	12 (18.2)	48 (72.7)	5 (7.6)	1 (1.5)
	Piperacillin	0	1 (1.5)	55 (83.3)	10 (15.2)
	Carbapenem	0	0	52 (78.8)	14 (21.2)
IV Fluids					
	Crystalloids	66 (100)	0	0	0
	Colloids	14 (21.2)	49 (74.2)	3 (4.5)	0
Blood Products					
	Red Blood Cells (n=65)	23 (35.4)	41 (62.1)	1 (1.5)	0
	Fresh Frozen Plasma (n=63)	0	4 (6.3)	54 (85.7)	5 (7.9)
	Platelets (n=63)	0	2 (3.2)	58 (92.1)	3 (4.8)
Cardiovascular Drugs (*n* =65)					
	Noradrenaline	5 (7.7)	0	59 (90.8)	1 (1.5)
	Dopamine	4 (6.2)	12 (18.5)	12 (73.8)	1 (1.5)
	Dobutamine	0	5 (7.7)	54 (83.1)	6 (9.2)
	Adrenaline	36 (55.4)	29 (44.6)	0	0
	Hydrocortisone (n=66)	51 (77.3)	15 (22.7)	0	0
	Vasopressin	1 (1.5)	1 (1.5)	52 (80)	11 (16.9)
Anesthetic/Sedative Drugs (*n* =65)					
	Thiopentone	14 (21.5)	18 (27.7)	33 (50.8)	0
	Propofol	2 (3.1)	20 (30.8)	42 (64.6)	1 (1.5)
	Succinylcholine	10 (15.4)	19 (29.2)	36 (55.4)	0
	ND Muscle Relaxant	9 (14.1)	18 (28.1)	37 (57.8)	0
	IV opiate/opioid	11 (16.9)	34 (52.3)	20 (30.8)	0
	Diazepam	60 (92.3)	4 (6.2)	1 (1.5)	0
	Midazolam	2 (3.1)	19 (29.2)	43 (66.2)	1 (1.5)
Others					
	Insulin	25 (37.9)	40 (60.6)	1 (1.5)	0
	Heparin or LMWH (n=65)	4 (6.2)	53 (81.5)	8 (12.3)	0
	H2-Blockers (n=65)	6 (9.2)	38 (58.5)	17 (26.2)	4 (6.2)
	Proton Pump Inhibitor (n=65)	6 (9.2)	34 (52.3)	22 (33.8)	3 (4.6)
	Activated Protein C (n=65)	0	0	52 (80)	13 (20)

ND, non-depolarizing; IV, intravenous; LMWH, low molecular weight heparin; H2, histamine receptor 2.

All data are given as absolute values and percentages.

Table 2. Availability of Drugs to Provide Adequate Sepsis Care and Implement the Surviving Sepsis Campaign Guidelines

		Always	*Sometimes*	*Never*	*Don't Know*
Oxygen (*n* =65)		23 (35.4)	16 (24.2)	26 (39.4)	0
Antibiotics					
	Ampicillin	65 (98.5)	1 (1.5)	0	0
	Gentamycin	45 (68.2)	21 (31.8)	0	0
3rd /4th	*Gen Cephalosporin*	12 (18.2)	48 (72.7)	5 (7.6)	1 (1.5)
	Piperacillin	0	1 (1.5)	55 (83.3)	10 (15.2
	Carbapenem	0	0	52 (78.8)	14 (21.2
IV Fluids					
	Crystalloids	66 (100)	0	0	0
	Colloids	14 (21.2)	49 (74.2)	3 (4.5)	0
Blood Products					
	Red Blood Cells (n=65)	23 (35.4)	41 (62.1)	1 (1.5)	0
	Fresh Frozen Plasma (n=63)	0	4 (6.3)	54 (85.7)	5 (7.9)
	Platelets (n=63)	0	2 (3.2)	58 (92.1)	3 (4.8)
Cardiovascular Drugs (*n* =65)					
	Noradrenaline	5 (7.7)	0	59 (90.8)	1 (1.5)
	Dopamine	4 (6.2)	12 (18.5)	12 (73.8)	1 (1.5)
	Dobutamine	0	5 (7.7)	54 (83.1)	6 (9.2)
	Adrenaline	36 (55.4)	29 (44.6)	0	0
	Hydrocortisone (n=66)	51 (77.3)	15 (22.7)	0	0
	Vasopressin	1 (1.5)	1 (1.5)	52 (80)	11 (16.9
Anesthetic/Sedative Drugs (*n* =65)					
	Thiopentone	14 (21.5)	18 (27.7)	33 (50.8)	0
	Propofol	2 (3.1)	20 (30.8)	42 (64.6)	1 (1.5)
	Succinylcholine	10 (15.4)	19 (29.2)	36 (55.4)	0
	ND Muscle Relaxant	9 (14.1)	18 (28.1)	37 (57.8)	0
	IV opiate/opioid	11 (16.9)	34 (52.3)	20 (30.8)	0
	Diazepam	60 (92.3)	4 (6.2)	1 (1.5)	0
	Midazolam	2 (3.1)	19 (29.2)	43 (66.2)	1 (1.5)
Others					
	Insulin	25 (37.9)	40 (60.6)	1 (1.5)	0
	Heparin or LMWH (n=65)	4 (6.2)	53 (81.5)	8 (12.3)	0
	H2-Blockers (n=65)	6 (9.2)	38 (58.5)	17 (26.2)	4 (6.2)
	Proton Pump Inhibitor (n=65)	6 (9.2)	34 (52.3)	22 (33.8)	3 (4.6)
	Activated Protein C (n=65)	0	0	52 (80)	13 (20)

ND, non-depolarizing; IV, intravenous; LMWH, low molecular weight heparin; H2, histamine receptor 2.

All data are given as absolute values and percentages.

Table 3. Availability of Equipment to Provide Adequate Sepsis Care and Implement the Surviving Sepsis Campaign Guidelines

	Always	*Sometimes*	*Never*	*Don't Know*
Diagnostic Equipment (*n*=63)				
X-ray	39 (61.9)	1 (1.6)	23 (36.5)	0
Ultrasound	24 (38.1)	6 (9.5)	33 (52.4)	0
Echocardiography	0	0	57 (90.5)	6 (9.5)
Laboratory Investigations (*n*=62)				
Gram Stain (n=63)	59 (93.7)	4 (6.3)	0	0
Microbiological Cultures	12 (19.4)	11 (17.7)	38 (61.3)	1 (1.6)
Antibiotic Sensitivities	9 (14.5)	11 (17.7)	40 (64.5)	2 (3.2)
Blood Sugar	32 (51.6)	28 (45.2)	2 (3.2)	0
Blood Gas Analysis	1 (1.6)	8 (12.9)	53 (85.5)	0
Lactate	0	5 (8.1)	55 (88.7)	2 (3.2)
Blood Count	4 (6.5)	21 (33.9)	37 (59.7)	0
Creatinine	9 (14.5)	6 (9.7)	47 (75.8)	0
Bilirubin	8 (12.7)	7 (11.3)	47 (75.8)	0
Prothrombin Time/INR	4 (6.5)	0	55 (88.7)	3 (4.8)
Other Coagulation Tests	16 (25.8)	41 (66.1)	5 (8.1)	0
Monitoring Equipment (*n*=65)				
Body Temperature	62 (95.4)	3 (4.6)	0	0
Non-Invasive Blood Pressure	63 (96.9)	2 (3.1)	0	0
Invasive Blood Pressure	0	1 (1.5)	54 (83.1)	10 (15.4)
Oxygen Saturation	9 (13.8)	34 (52.3)	21 (32.3)	1 (1.5)
Central Venous Pressure	0	0	57 (87.7)	8 (12.3)
Cardiac Output	0	0	58 (89.2)	7 (10.8)
Pulmonary Arterial Pressure	0	0	60 (92.3)	5 (7.7)
Endtidal Carbon Dioxide	0	11 (16.9)	48 (73.8)	6 (9.2)
Other Equipment (*n*=63)				
Mechanical Ventilator	0	2 (3.2)	60 (95.2)	1 (1.6)
Syringe Pump	0	3 (4.8)	57 (90.5)	3 (4.8)
Fluid Infuser	0	2 (3.2)	58 (92.1)	3 (4.8)
Peritoneal Dialysis	0	0	56 (88.9)	7 (11.1)
Haemodialysis/Haemofiltration	0	0	56 (88.9)	7 (11.1)

INR, international normalized ratio.
All data are given as absolute values and percentages.

Table 4. Availability of Disposable Material to Provide Adequate Sepsis Care And Implement the Surviving Sepsis Campaign Guidelines

	Always	*Sometimes*	*Never*	*Don't Know*
Disposable Material (*n*=65)				
IV Cannula	63 (96.9)	2 (3.1)	0	0
IV Fluid Giving Set	65 (100)	0	0	0
Urinary Catheter	46 (70.8)	19 (29.2)	0	0
Nasogastric Tube	39 (60)	25 (38.5)	1 (1.5)	0
Endotracheal Tube	20 (30.8)	18 (27.7)	27 (41.5)	0
Oxygen Face Mask	19 (29.7)	20 (31.3)	25 (39.1)	0
Oxygen Nasal Cannula	17 (26.6)	22 (34.4)	25 (39.1)	0
Central Venous Catheter	2 (3.1)	3 (4.6)	58 (89.2)	2 (3.1)
Antithrombotic Stockings (n=60)	8 (13.3)	10 (16.7)	27 (45)	15 (25)

IV, intravenous.
All data are given as absolute values and percentages.

Table 5. Ability to Implement the Surviving Sepsis Campaign Guidelines

n		66
Ability to Implement the SSC Guidelines	*n (%)*	0
Percentage of Implementable Recommendations/Suggestions	*(%)*	32 (29-37)
Ability to Implement All Level I Recommendations	*n (%)*	0
Percentage of Implementable Level I Recommendations	*(%)*	46 (44-54)
Ability to Implement All Level IA and IB Recommendations	*n (%)*	0
Percentage of Implementable Level IA and IB Recommendations	*(%)*	50 (46-54)
Ability to Implement All Level IC and ID Recommendations	*n (%)*	0
Percentage of Implementable Level IC and ID Recommendations	*(%)*	42 (42-54)
Ability to Implement All Level II Suggestions	*n (%)*	0
Percentage of Implementable Level II Suggestions	*(%)*	22 (17-22)

SSC, Surviving Sepsis Campaign.
Data are given as median values with interquartile ranges, if not otherwise indicated.

to those not addressed, our results indicate a striking shortage of key hospital facilities and resources to provide adequate care for sepsis patients. On average, resources were only available to implement one third of recommendations/suggestions of the life-saving SSC guidelines. This number is even more alarming considering that about 25% of SSC recommendations/ suggestions are passive ("do not use") and do not require resources[15]. While relevant shortages of medical equipment and supplies were reported from other Sub-Sahara African countries[19-22], the situation appears particularly devastating in Eastern DRC.

Despite of the overall lack of resources, the shortage of some specific materials is particularly concerning. For example, only about one third of respondents stated that oxygen was constantly available at their hospital. Hypoxaemia and tissue hypoxia plays a central role in the pathophysiology of sepsis[4]. Similarly, not a single respondent claimed to have consistent access to broad-spectrum antibiotics such as piperacillin or carbapenems. Less than one fifth had third/fourth generation cephalosporins always available. Adequate antibiotic coverage with or without surgical source control is the mainstay of sepsis therapy[4,26]. A high prevalence of microbial resistance against penicillins and aminoglycosides in Sub-Sahara Africa[27] may render the few constantly available antibiotics of little benefit for patients suffering from sepsis. Accordingly, a prospective observational study of the management and outcome of sepsis in two Ugandan hospitals observed no survival benefit of administering empiric antibiotics or administering any antibiotic within one hour after presentation[10]. Epinephrine is an integral drug for the management of patients with shock or cardiac arrest, but was reported to be constantly available in only half of the surveyed hospitals. Finally, diagnostic devices are fundamental for diagnosing and identifying the infectious source. The widespread lack of reliable x-ray and sonography machines in the analyzed hospitals may result in delayed or failed recognition of the source of infection in sepsis patients.

Given that the SSC guidelines reflect the current best practice of sepsis management[15], it is clear from our results that a lack of resources to implement these guidelines may inevitably result in inadequate sepsis care. Yet, our data cannot prove a cause-effect relationship between lacking resources to provide adequate sepsis care and the excess mortality arising from infectious diseases in the Eastern DRC. It is very likely that additional factors contribute to high fatality rates associated with infection and sepsis in this region. Our survey indicated that key hospital facilities to treat sepsis patients such as emergency departments or intensive care units do not exist in the majority of the analyzed hospitals. Insufficient staffing prevents consistent implementation of the SSC guidelines into clinical practice even in high-income countries[28]. Lack of health care workers is a well-known and widespread problem in Sub-Sahara Africa[29] and the DRC[30]. So far, less than 100 physicians have been trained as anesthesiologists in the DRC (unpublished data). Accordingly, the fact that >90% of respondents in this survey were non-physicians implies that the level of education of health care providers caring for acutely and critically ill patients, such as those suffering from sepsis, may be insufficient.

What could be realistic options to improve the management of sepsis patients in the Eastern DRC or other resource poor areas? Based on our survey results, sepsis guidelines should be adapted to target the few available resources to be used according to the latest clinical evidence. This may be particularly relevant for therapeutic interventions with a high chance of improving patient survival such as those included in level IA and IB recommendations of the SSC guidelines. On average, respondents had resources constantly available to implement 50% of level IA and IB recommendations suggesting that guideline adaption based on locally available resources may allow implementation of a reasonable number of life-saving interventions into the care of sepsis patients. However, given the striking shortage of resources detected in this survey, adaption of guidelines alone will most likely not compensate for the lack of essential resources. Resources such as oxygen, broad-spectrum antibiotics, epinephrine and diagnostic devices are indispensable and vital resources which need to be supplied to health care facilities in order to improve the care and outcome of septic patients. Availability of these resources, especially oxygen and epinephrine, carries a high potential to advance the care of other acutely and critically ill patients as well. As mentioned

above, establishment of emergency and intensive care departments, adequate staffing and training of health care providers may be further possibilities to improve the management of patients suffering from severe infection in the Eastern DRC.

Some limitations need to be considered when interpreting our study results. Apart from the impossibility of evaluation of all hospitals in the Eastern DRC (for reasons stated above), our survey investigated the availability of resources in a binary fashion and might therefore have missed quantitative shortages in the few constantly available resources. This could, for example, be relevant for the availability of fluids. Although all respondents stated to have crystalloid solutions constantly available at their hospital, data from the same area showed that the amount of intraoperatively available fluids was rationed[31]. Secondly, although the questionnaire used in this survey underwent pilot testing and has been used in another setting before, no assessment of test-retest reliability and inter-observer variability was performed. Together with the lack of clinical sensibility testing of the survey instrument, this limits the validity of our results[32]. Third, our survey did not assess the availability of resources necessary to manage children with sepsis. Since special sized disposable materials and equipment are required, it is likely that resources needed to care for critically ill children with sepsis are even less frequently available in the Eastern DRC. This may be of particular relevance considering that children account for nearly 50% of deaths although they comprise only 19% of the population in this region[13].

In conclusion, our survey indicates a critical shortage of resources required to provide adequate sepsis care and implement the SSC guidelines in a cluster of hospitals in the Eastern DRC. While adaption of current guidelines may help to target available resources according to the latest clinical evidence, this may not be sufficient to compensate for the shortage of indispensable resources such as oxygen, broad-spectrum antibiotics, epinephrine and diagnostic devices. These essential components of sepsis care need to be provided to improve sepsis care in the Eastern DRC.

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ESM Fig. 1
Study Questionnaire in its original version in English language

1. GENERAL INFORMATION

Name of your hospital? .....

Country where hospital situated? .....

Type of hospital? ○District ○Regional/Provincial ○University ○Private ○Other (please write) .....

Number of hospital beds? .....

What is your grade? ○ Physician Anaesthetist ○ Other Physician
○ Non-Physician Anaesthetist ○ Other (please write) .....

2. HOSPITAL FACILITIES

Does your hospital have the following?

	Yes	No	Don't know
Emergency / resuscitation room (Room for emergency patient who's just arrived to hospital)	○	○	○
Intensive care unit (Dedicated unit for critically ill patients)	○	○	○
Operating Theatre	○	○	○

3. DRUGS

Are the following drugs available in your hospital?

	Always	Sometimes	Never	Don't know
IV Ampicillin	○	○	○	○
IV Gentamycin	○	○	○	○
IV Ceftriaxone, Cefotaxime or Ceftazidime	○	○	○	○
IV Piperacillin	○	○	○	○
IV Meropenem or other carbapenem	○	○	○	○
IV Hydrocortisone	○	○	○	○
Sodium Chloride, Ringers Lactate or other crystalloid	○	○	○	○
Gelatine, Dextran or other Colloid	○	○	○	○
Insulin	○	○	○	○
Oxygen	○	○	○	○
Blood Transfusion	○	○	○	○
Fresh Frozen Plasma	○	○	○	○
Platelets	○	○	○	○
Heparin or Low Molecular Weight Heparin	○	○	○	○
Ranitidine or other H2 receptor blocker	○	○	○	○
Omeprazole or other Proton Pump Inhibitor	○	○	○	○
IV morphine, pethidine or other IV opioid	○	○	○	○
Diazepam	○	○	○	○
Midazolam	○	○	○	○
Propofol	○	○	○	○
Thiopentone	○	○	○	○
Succinylcholine	○	○	○	○
Atracurium or other non-depolarising muscle relaxant	○	○	○	○
Noradrenaline	○	○	○	○
Dopamine	○	○	○	○
Dobutamine	○	○	○	○
Adrenaline	○	○	○	○
Vasopressin	○	○	○	○
Activated Protein C	○	○	○	○

4. PATIENT MONITORING

Can the following variables be monitored in your hospital?

	Always	Sometimes	Never	Don't know
Temperature	○	○	○	○
Non-invasive blood pressure	○	○	○	○
Invasive arterial blood pressure	○	○	○	○
Oxygen saturation	○	○	○	○
Central venous pressure	○	○	○	○
Cardiac output	○	○	○	○
Pulmonary arterial pressure	○	○	○	○
End tidal CO_2	○	○	○	○

5. LABORATORY

Can the following investigations be done in your hospital?

	Always	Sometimes	Never	Don't know
Blood slide for malaria parasites	○	○	○	○
Direct microscopy & gram stain	○	○	○	○
Bacteria culture	○	○	○	○
Antibiotic sensitivities	○	○	○	○
Blood glucose	○	○	○	○
Arterial blood gases	○	○	○	○
Blood lactate	○	○	○	○
Full blood count	○	○	○	○
Creatinine	○	○	○	○
Bilirubin	○	○	○	○
Prothrombin Time (INR)	○	○	○	○
Other coagulation test	○	○	○	○

6. EQUIPMENT

Is the following equipment available in your hospital?

	Always	Sometimes	Never	Don't know
X-ray	○	○	○	○
Ultrasound - Abdomen	○	○	○	○
Echocardiography	○	○	○	○
Mechanical Ventilator	○	○	○	○
Syringe pump	○	○	○	○
Fluid infuser/Infusion pump	○	○	○	○
Peritoneal Dialysis	○	○	○	○
Hemodialysis/ hemofiltration	○	○	○	○

7. DISPOSABLES

Are the following items available in your hospital?

	Always	Sometimes	Never	Don't know
Venous cannula	○	○	○	○
IV fluid giving set	○	○	○	○
Urinary catheter	○	○	○	○
Gastric tube (NG-tube)	○	○	○	○
Endotracheal tube	○	○	○	○
Oxygen masks	○	○	○	○
Oxygen nasal cannula	○	○	○	○
Central venous catheter	○	○	○	○
Compression stockings	○	○	○	○

Thank you very much for participation!

ESM Table 1. Hospital facilities, equipment, drugs and disposable materials required to implement single recommendations/suggestions of the Surviving Sepsis Campaign guidelines.

I A - Initial resuscitation (first 6 hrs)

☐ Begin resuscitation immediately in patients with hypotension or elevated serum lactate 4 mmol/L; do not delay pending intensive care unit admission (1C)
Materials required: facility to monitor non-invasive or invasive arterial blood pressure and measure lactate levels, intensive care unit

☐ Resuscitation goals (1C)
Central venous pressure 8–12 mm Hg
Mean arterial pressure 65 mm Hg
Urine output 0.5 mL*kg-1*hr-1
Central venous (superior vena cava) oxygen saturation 70% or mixed venous 65%
Materials required: facility to monitor central venous pressure, facility to monitor non-invasive or invasive arterial blood pressure, availability of a urinary catheter, central venous catheter, and facility to measure blood gases

- If venous oxygen saturation target is not achieved (2C)

Consider further fluid
Transfuse packed red blood cells if required to hematocrit of 30% and/or
Start dobutamine infusion, maximum 20 μg kg-1 min-1
Materials required: central venous catheter, facility to measure blood gases, availability of IV cannula, IV fluid giving set, crystalloid or colloid solution, blood transfusion and dobutamine

I B - Diagnosis

☐ Obtain appropriate cultures before starting antibiotics provided this does not significantly delay antimicrobial administration (1C)
Obtain two or more blood cultures
One or more blood cultures should be percutaneous
One blood culture from each vascular access device in place 48 hrs
Culture other sites as clinically indicated
Materials required: direct microscopy and gram stain, bacteria culture

☐ Perform imaging studies promptly to confirm and sample any source of infection, if safe to do so (1C)
Materials required: availability of x-ray and ultrasound

I C - Antibiotic therapy

☐ Begin intravenous antibiotics as early as possible and always within the first hour of recognizing severe sepsis (1D) and septic shock (1B)
Materials required: availability of at least one antibiotic drug

☐ Broad-spectrum: one or more agents active against likely bacterial/fungal pathogens and with good penetration into presumed source (1B)
Materials required: availability of either ceftriaxone/cefotaxime/ceftazidime, piperacilline or meropenem/other carbapenem

☐ Reassess antimicrobial regimen daily to optimize efficacy, prevent resistance, avoid toxicity, and minimize costs (1C)
Materials required: none

- Consider combination therapy in *Pseudomonas* infections (2D)

Materials required: bacteria culture and availability of at least two of the following antibiotic drugs: ceftriaxone/cefotaxime/ceftazidime, piperacilline, meropenem/other carbapenem, or gentamycin

- Consider combination empiric therapy in neutropenic patients (2D)

Materials required: facility to measure full blood count and at least two antibiotic drugs

- Combination therapy 3–5 days and de-escalation following susceptibilities (2D)

Materials required: facility to determine antibiotic sensitivities

☐ Duration of therapy typically limited to 7–10 days; longer if response is slow or there are undrainable foci of infection or immunologic deficiencies (1D)
Materials required: none

☐ Stop antimicrobial therapy if cause is found to be noninfectious (1D)
Materials required: facility to perform bacteria cultures

I D - Source identification and control

☐ A specific anatomic site of infection should be established as rapidly as possible (1C) and within first 6 hrs of presentation (1D)
Materials required: availability of x-ray and ultrasound

☐ Formally evaluate patient for a focus of infection amenable to source control measures (e.g. abscess drainage, tissue debridement) (1C)
Materials required: availability of x-ray and ultrasound

☐ Implement source control measures as soon as possible following successful initial resuscitation (1C) (exception: infected pancreatic necrosis, where surgical intervention is best delayed) (2B)
Materials required: operation room

☐ Choose source control measure with maximum efficacy and minimal physiologic upset (1D)
Materials required: none

☐ Remove intravascular access devices if potentially infected (1C)
Materials required: none

I E - Fluid therapy

☐ Fluid-resuscitate using crystalloids or colloids (1B)
Materials required: availability of IV cannula, IV fluid giving set, crystalloid or colloid solution
☐ Target a central venous pressure of 8 mm Hg (12 mm Hg if mechanically ventilated) (1C)
Materials required: facility to measure central venous pressure
☐ Use a fluid challenge technique while associated with a hemodynamic improvement (1D)
Materials required: availability of IV cannula, IV fluid giving set, crystalloid or colloid solution and facility to monitor non-invasive or invasive arterial blood pressure
☐ Give fluid challenges of 1000 mL of crystalloids or 300–500 mL of colloids over 30 mins. More rapid and larger volumes may be required in sepsis-induced tissue hypoperfusion (1D)
Materials required: availability of IV cannula, IV fluid giving set, crystalloid or colloid solution
☐ Rate of fluid administration should be reduced if cardiac filling pressures increase without concurrent hemodynamic improvement (1D)
Materials required: availability of IV cannula, IV fluid giving set, crystalloid or colloid solution, facility to measure central venous pressure

I F - Vasopressors

☐ Maintain mean arterial pressure 65 mm Hg (1C)
Materials required: facility to measure non-invasive or invasive arterial blood pressure
☐ Norepinephrine and dopamine centrally administered are the initial vasopressors of choice (1C)
Materials required: availability of a central venous catheter, norepinephrine or dopamine
- Epinephrine, phenylephrine, or vasopressin should not be administered as the initial vasopressor in septic shock (2C). Vasopressin 0.03 units/min may be subsequently added to norepinephrine with anticipation of an effect equivalent to norepinephrine alone

Materials required: availability of vasopressin
- Use epinephrine as the first alternative agent in septic shock when blood pressure is poorly responsive to norepinephrine or dopamine (2B).

Materials required: facility to monitor non-invasive or invasive arterial blood pressure, availability of epinephrine
☐ Do not use low-dose dopamine for renal protection (1A)
Materials required: none
☐ In patients requiring vasopressors, insert an arterial catheter as soon as practical (1D)
Materials required: facility to monitor invasive arterial blood pressure

I G - Inotropic therapy

☐ Use dobutamine in patients with myocardial dysfunction as supported by elevated cardiac filling pressures and low cardiac output (1C)
Materials required: facility to monitor central venous pressure or cardiac output, availability of dobutamine
☐ Do not increase cardiac index to predetermined supranormal levels (1B)
Materials required: none

I H - Corticosteroids

- Consider intravenous hydrocortisone for adult septic shock when hypotension responds poorly to adequate fluid resuscitation and vasopressors (2C)

Materials required: facility to measure non-invasive or invasive arterial blood pressure, availability of IV cannula, IV fluid giving set, availability of crystalloid or colloid solution, availability of a central venous catheter, dopamine or norepinephrine, hydrocortisone
- ACTH stimulation test is not recommended to identify the subset of adults with septic Shock who should receive hydrocortisone (2B)

Materials required: none
- Hydrocortisone is preferred to dexamethasone (2B)

Materials required: availability of hydrocortisone
- Fludrocortisone (50 g orally once a day) may be included if an alternative to hydrocortisone is being used that lacks significant mineralocorticoid activity. Fludrocortisone is optional if hydrocortisone is used (2C)

Materials required: none
- Steroid therapy may be weaned once vasopressors are no longer required (2D)

Materials required: availability of hydrocortisone, availability of a central venous catheter, dopamine or norepinephrine
☐ Hydrocortisone dose should be 300 mg/day (1A)
Materials required: availability of hydrocortisone
☐ Do not use corticosteroids to treat sepsis in the absence of shock unless the patient's endocrine or corticosteroid history warrants it (1D)
Materials required: none

I I - Recombinant human activated protein C (rhAPC)

- Consider rhAPC in adult patients with sepsis-induced organ dysfunction with clinical assessment of high risk of death (typically APACHE II 25 or multiple organ failure) if there are no contraindications (2B, 2C for postoperative patients).

Materials required: facility to measure body temperature, non-invasive or invasive arterial blood

pressure, arterial blood gases, creatinine, and full blood count, availability of recombinant human activated protein C

☐ Adult patients with severe sepsis and low risk of death (typically, APACHE II 20 or one organ failure) should not receive rhAPC (1A)

Materials required: facility to measure body temperature, non-invasive or invasive arterial blood pressure, arterial blood gases, creatinine, and full blood count

I J - Blood product administration

☐ Give red blood cells when hemoglobin decreases to 7.0 g/dL (70 g/L) to target a hemoglobin of 7.0–9.0 g/dL in adults (1B). A higher hemoglobin level may be required in special circumstances (e.g., myocardial ischaemia, severe hypoxemia, acute hemorrhage, cyanotic heart disease, or lactic acidosis)

Materials required: facility to measure full blood count, availability of IV cannula, IV fluid giving set and blood transfusion

o Do not use erythropoietin to treat sepsis-related anemia. Erythropoietin may be used for other accepted reasons (1B)

Materials required: none

o Do not use fresh frozen plasma to correct laboratory clotting abnormalities unless there is bleeding or planned invasive procedures (2D)

Materials required: availability of IV cannula, IV fluid giving set and fresh frozen plasma

☐ Do not use antithrombin therapy (1B)

Materials required: none

o Administer platelets when (2D)

Counts are 5000/mm3 (5 x 10^9/L) regardless of bleeding

Counts are 5000–30,000/mm3 (5–30 x 10^9/L) and there is significant bleeding risk

Higher platelet counts (50,000/mm3 [50 x 10^9/L]) are required for surgery or invasive procedures

Materials required: availability of IV cannula, IV fluid giving set and platelets

II A - Mechanical ventilation of sepsis-induced ALI/ARDS

☐ Target a tidal volume of 6 mL/kg (predicted) body weight in patients with ALI/ARDS (1B)

Materials required: facility to measure oxygen saturation or arterial blood gases, availability of endotracheal tube and mechanical ventilator

☐ Target an initial upper limit plateau pressure 30 cmH2O. Consider chest wall compliance when assessing plateau pressure (1C)

Materials required: availability of endotracheal tube and mechanical ventilator

☐ Allow PaCO2 to increase above normal, if needed, to minimize plateau pressures and tidal volumes (1C)

Materials required: facility to measure arterial blood gases or endtidal CO_2, availability of endotracheal tube and mechanical ventilator

☐ Set PEEP to avoid extensive lung collapse at end-expiration (1C)

Materials required: availability of endotracheal tube and mechanical ventilator

o Consider using the prone position for ARDS patients requiring potentially injurious levels of FIO2 or plateau pressure, provided they are not put at risk from positional changes (2C)

Materials required: availability of endotracheal tube and mechanical ventilator

☐ Maintain mechanically ventilated patients in a semirecumbent position (head of the bed raised to 45°) unless contraindicated (1B), between 30° and 45° (2C)

Materials required: none

o Noninvasive ventilation may be considered in the minority of ALI/ARDS patients with mild to moderate hypoxemic respiratory failure. The patients need to be hemodynamically stable, comfortable, easily arousable, able to protect/clear their airway, and expected to recover rapidly (2B)

Materials required: facility to monitor oxygen saturation or arterial blood gases and non-invasive or invasive arterial blood pressure, availability of mechanical ventilator

☐ Use a weaning protocol and an SBT regularly to evaluate the potential for discontinuing mechanical ventilation (1A)

Materials required: availability of endotracheal tube and mechanical ventilator

☐ Spontaneous breathing trial options include a low level of pressure support with continuous positive airway pressure 5 cm H2O or a T piece

Materials required: availability of endotracheal tube and mechanical ventilator

☐ Before the spontaneous breathing trial, patients should

be arousable

be hemodynamically stable without vasopressors

have no new potentially serious conditions

have low ventilatory and end-expiratory pressure requirement

require FiO2 levels that can be safely delivered with a face mask or nasal cannula

Materials required: facility to monitor non-invasive or invasive arterial blood pressure, availability of endotracheal tube and mechanical ventilator, oxygen, oxygen mask or nasal cannula

☐ Do not use a pulmonary artery catheter for the routine monitoring of patients with ALI/ARDS (1A)

Materials required: none

☐ Use a conservative fluid strategy for patients with established ALI who do not have evidence of tissue

hypoperfusion (1C)
Materials required: availability of IV cannula, IV fluid giving set, crystalloid or colloid solution

II B - Sedation, analgesia, and neuromuscular blockade in sepsis
☐ Use sedation protocols with a sedation goal for critically ill mechanically ventilated patients (1B)
Materials required: none
☐ Use either intermittent bolus sedation or continuous infusion sedation to predetermined end points (sedation scales), with daily interruption/lightening to produce awakening. Re-titrate if necessary (1B)
Materials required: availability of IV morphine/opioid, benzodiazepine, propofol or thiopentone
☐ Avoid neuromuscular blockers where possible. Monitor depth of block with train-of-four when using continuous infusions (1B)
Materials required: availability of non-depolarizing muscle relaxant

II C - Glucose control
☐ Use intravenous insulin to control hyperglycemia in patients with severe sepsis following stabilization in the ICU (1B)
Materials required: facility to measure blood glucose, availability of insulin
☐ Aim to keep blood glucose 150 mg/dL (8.3 mmol/L) using a validated protocol for insulin dose adjustment (2C)
Materials required: facility to measure blood glucose, availability of insulin
☐ Provide a glucose calorie source and monitor blood glucose values every 1–2 hrs (4 hrs when stable) in patients receiving intravenous insulin (1C)
Materials required: facility to measure blood glucose, availability of insulin
☐ Interpret with caution low glucose levels obtained with point of care testing, as these techniques may overestimate arterial blood or plasma glucose values (1B)
Materials required: facility to measure blood glucose

II D - Renal replacement
- Intermittent hemodialysis and continuous veno-venous hemofiltration are considered equivalent (2B)

Materials required: availability of hemodialysis or hemofiltration
- Continuous veno-venous hemofiltration offers easier management in hemodynamically unstable patients (2D)

Materials required: facility to measure non-invasive or invasive arterial blood pressure, availability of hemodialysis or hemofiltration

II E - Bicarbonate therapy
☐ Do not use bicarbonate therapy for the purpose of improving hemodynamics or reducing vasopressor requirements when treating hypoperfusion-induced lactic acidemia with pH 7.15 (1B)
Materials required: none

II F - Deep vein thrombosis prophylaxis
☐ Use either low-dose unfractionated heparin or low molecular weight heparin, unless contraindicated (1A)
Materials required: availability of unfractionated or low molecular weight heparin
☐ Use a mechanical prophylactic device, such as compression stockings or an intermittent compression device, when heparin is contraindicated (1A)
Materials required: availability of compression stockings
- Use a combination of pharmacologic and mechanical therapy for patients who are at very high risk for deep vein thrombosis (2C)

Materials required: availability of unfractionated or low molecular weight heparin and compression stockings
- In patients at very high risk, low molecular weight heparin should be used rather than unfractionated heparin (2C)

Materials required: availability of low molecular weight heparin

II G - Stress ulcer prophylaxis
☐ Provide stress ulcer prophylaxis using H2 blocker (1A) or proton pump inhibitor (1B). Benefits of prevention of upper gastrointestinal bleed must be weighed against the potential for development of ventilator-acquired pneumonia
Materials required: availability of ranitidine/other H2 blocker or omeprazole/other proton pump inhibitor

II I - Consideration for limitation of support
☐ Discuss advance care planning with patients and families. Describe likely outcomes and set realistic expectations (1D)
Materials required: none