UNIVERSITY of RWANDA

IMPACT OF "quick SEQUENTIAL ORGAN FAILURE ASSESSMENT" (qSOFA) AT ADMISSION TO THE INTENSIVE CARE UNIT ON HOSPITAL OUTCOME FOR CRITICALLY ILL PATIENT AT KIGALI UNIVERSITY TEACHING HOSPITAL.

By

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Research work submitted in partial fulfilment of the requirements for the award of the Degree of Master of Medicine in Anaesthesiology.

Department of Anesthesiology, Critical Care and Emergency

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Kigali October, 2021

DECLARATION AND AUTHORITY TO SUBMIT THE DISSERTATION

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Title of the project: ***IMPACT OF "quick SEQUENTIAL ORGAN FAILURE ASSESSMENT" qSOFA AT ADMISSION TO THE INTENSIVE CARE UNIT ON HOSPITAL OUTCOME FOR CRITICALLY ILL PATIENT AT KIGALI UNIVERSITY TEACHING HOSPITAL.***

a. *Declaration by the Student*

I do hereby declare that this ***dissertation*** submitted in partial fulfillment of the requirements for the degree of **MASTERS OF SCIENCE** in **Anesthesiology, Critical Care and Emergency**, at the University of Rwanda/College of Medicine and Health Sciences, is my original work and has not previously been submitted elsewhere. Also, I do declare that a complete list of references is provided indicating all the sources of information quoted or cited.

Date and Signature of the Student

MBAHIRE Remy Steve....  21 July 2021

b. *Authority to Submit the dissertation*

In my capacity as a Supervisor, I do hereby authorize the student to submit his dissertation.

Prof. Paulin RUHATO BANGUTI

Signature: ...  ... Date: 29 July 2021

ABSTRACT

Background

Sepsis is a significant cause of morbidity and mortality worldwide with an increasing incidence. The qSOFA is used as a screening tool for sepsis in developed countries. This study aims to determine the impact of qSOFA in the prediction of outcome in adult patients admitted to the ICU of Kigali University Teaching Hospital (CHUK), with or without a suspected infection.

Methodology.

Data of adult patients admitted in ICU of CHUK were retrospectively and prospectively collected from May 2019 to December 2020.

I entered data in Epi-Info version 3 then defined high versus low-risk groups according to their qSOFA scores. I calculated raw mortality and prognostic performance values for both risk groups and analyzed AUROC as primary outcome and average ICU length of stay and post- ICU discharge mortality rate as secondary outcome.

Results:

The study consisted of 148 participants. One hundred and forty one were enrolled for analysis with 40 (28.4%) in the high-risk group (qSOFA score ≥2) and 101 (71.6%) in the low-risk group. The median age was 33 (IQR: 24-41.5) for the high-risk group, which was significantly smaller than the median age of 40 (IQR: 31-59) for the low-risk group ($Z=2.55$, $p<0.05$). Altered mentation was the main reason of admission with 32 (80%) cases with GCS <15 in the high-risk group and 40 (40%) in the low-risk group. ICU and post-ICU discharge mortality rate in the high-risk vs. low-risk group was 20% and 0% vs. 19.6% and 3.5% respectively. The prognostic performance value of the qSOFA score (with a cutoff of 2) in predicting ICU mortality consisted of 29% sensitivity, 73% specificity, 21% positive predictive value, and 80% negative predictive value. The area under the receiver operating characteristic curve was 0.555 (95% CI -.528-0.589). The median ICU length of stay was 6 days (IQR 2-10) and 5 days (IQR 3-11) for the high-risk vs. low-risk group with an absolute difference of 2.89 (95% CI -1.83 to 7.62, p-value 0.118).

Conclusion:

Following the index study it was found that the qSOFA score was a poor predictor of ICU outcomes in this setting.

Key words: Sepsis, quick Sequential Organ Failure Assessment, Intensive care Unit.

DEDICATION

To the Almighty God

To my wife and children

To my uncle and grandmothers

To my sister and friends

To my classmates and other peoples who contributed to this study

I dedicate this work.

ACKNOWLEDGEMENTS

The achievement of this work resulted from effort of many people to whom I am expressing my feelings of gratitude.

This dissertation would have never been accomplished without the tireless guidance and mentorship of Prof Paulin RUHATO BANGUTI and Prof Marcel DURIEUX; I express my deepest appreciation to them.

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LIST OF ACRONYMS and ABBREVIATIONS

AUROC: Area Under the Receiver Operating characteristic Curve

bpm: breaths per minute

CHUB: Butare University Teaching Hospital

CHUK: Kigali University Teaching Hospital

CI: Confidence Interval

CMHS: College of Medicine and Health Sciences

GCS: Glasgow Coma Scale

HDU: High Dependency Unit

HIC: High Income Country

ICU: Intensive Care Unit

IRB: Institutional Review Board

LMIC: Low and Middle Income Country

MEOWS: Modified Early Obstetric Warning Score

mmHg: millimetre of mercury

qSOFA: quick Sequential Organ Failure Assessment

ROC: Receiver Operating Characteristic Curve

SD: Standard Deviation

SIRS: Systemic Inflammatory Response Syndrome

SOFA: Sequential Organ Failure Assessment

UR: University of Rwanda.

CHAPTER I. INTRODUCTION

I.1. Background

Sepsis is a significant cause of morbidity and mortality worldwide, with an incidence of 240 cases per 100,000 population in high income countries (HIC) and more than 19 million sepsis cases and 5 million sepsis-related deaths estimated to occur annually—the majority in low and middle-income countries (LMICs). ICU and hospital mortality rates in patients with sepsis reported as 25.8% worldwide; 47.2% in Africa; 29.1% in Rwanda (1–5).

Despite the significant burden and poor outcomes of this critical illness in LMIC, few studies have been published defining intensive care management strategies settings (1,6).

Sepsis is currently defined as life-threatening acute organ dysfunction secondary to a dysregulated host response to infection. To improve the identification of patients at risk for clinical deterioration from infection, the Third International Consensus definition for sepsis and septic shock (Sepsis-3) recommends a quick scoring system, the "quick sequential organ failure assessment score" (qSOFA), comprises 3 elements assessed at the bedside (altered mental status with a Glasgow Coma Scale (GCS) <15, respiratory rate ≥22 bpm, and systolic blood pressure <100 mmHg) and without the need for laboratory tests. Patients who show abnormalities of 2 out of 3 elements are considered at risk for clinical deterioration and therefore early intervention should be initiated during the first hour of recognition (7–9).

The qSOFA is used as a screening tool for sepsis in developed countries and helps to identify patients at higher risk for excess hospital mortality among adults with suspected infection. However, there is limited information on the epidemiology of sepsis in low and middle-income countries (LMIC), including Rwanda. It is not clear that prognostication tools validated in developed countries are applicable to resource-constrained settings. Many factors may alter the utility of the tool in a setting like Rwanda; some examples include differences in comorbidities, genetic background, nutritional status, and therapeutic options available in the ICU (10).

The ICU of Kigali University Teaching Hospital (CHUK) receives medical as well as surgical critically ill patients with variable indications for admission: About 41.9% of Rwandan patients at two major teaching hospitals in Rwanda were diagnosed with sepsis within 24hours of ICU admission, 33.2% with severe sepsis, and 20.9% with septic shock. Frequently, the

diagnosis of infection is often made late and each of these diagnosis was associated with higher mortality ($p < 0.001$, respectively)(11). We therefore hypothesized that early application of qSOFA, before a specific condition is considered would help to reduce mortality. This study aims to determine the impact of qSOFA in the prediction of outcome in all patients admitted to the ICU of CHUK, with or without a suspected infection.

I.2. Study objectives:

I.2.1. General Objective:

To determine the impact of qSOFA score at admission to ICU in predicting hospital outcomes for critically ill patients at CHUK.

I.2.2. Specific objectives:

To determine the distribution of qSOFA scores for patients admitted to ICU at CHUK.

To analyse the ability of qSOFA in predicting mortality and ICU length of stay.

I.3. Research question

Does the distribution of qSOFA scores for patients admitted to ICU predict their risk of clinical status deterioration?

Is the qSOFA reliable in predicting mortality and ICU length of stay at CHUK?

I.4. Significance of the study

Sepsis is among high leading causes of morbidity and mortality worldwide with an increasing incidence. It is not clear that screening tools validated in developed countries are useful in limited settings. Many factors, including differences in comorbidities, nutritional status, and therapeutic options available in the ICU may alter the utility of the tool in a setting like Rwanda. We therefore want to determine whether using the qSOFA score predict outcome of the patients admitted in ICU at CHUK.

I.5. Definition of concepts operational meaning.

qSOFA: also known as quick Sequential Organ Failure Assessment. It is defined by three criteria derived from three major organs used in the original SOFA score as follows: acute respiratory failure defined by an increased respiratory rate superior to 22 bpm, altered mentation with a GCS<15 and a low blood pressure as a systolic blood pressure less than 100mmHg (Singer M. 2016).

Sepsis: is defined as presence of presumed infection with life-threatening organ dysfunction caused by a dysregulated response of the host to the presence of an infection materialized most of the time by fever, elevated WBC and/or presence of pus(7).

ICU: also known as critical care unit. It is a multidisciplinary and Inter-professional unity dedicated to the comprehensive management of patients having, or at risk of developing, acute, life threatening organ dysfunction. Intensive care uses an array of technologies that provide support of failing organ systems, particularly the lungs, cardiovascular system, and kidneys (12).

I.6. Structure and organization of the study

This study report is organized into two main parts; the first part consists of title page, abstract, dedication, acknowledgements, table of content, list of figures and tables and list of acronyms and abbreviations. The second part consists of six chapters. Chapter one includes the introduction, background, aims of the study, research objectives and questions, significance of the study, definition of concepts, structure/organization of the study. Chapter two reviews the theoretical and empirical literature of the topic. Chapter three is the methodology that includes research design, research approach, research setting, population, sampling, data collection process, data analysis methods, ethical considerations, data management, data dissemination, limitations and challenges to the study. Chapter four is made of introduction, demographic characteristics of respondents, presentation of results. Chapter five is composed of discussions, while the sixth is made of conclusion and recommendations.

CHAPTER II. LITERATURE REVIEW

II.1. Introduction

This chapter depicts the extensive literature on qSOFA. It is made of theoretical literature review including definition, parameters as well as interpretation of qSOFA and empirical literature review. The recent quantitative and qualitative research is explored to provide the current and consistent literature. Search engines used are Medline, Pub Med, Google Scholar and HINARI.

II.2. Theoritical literature review

II.2.1. Definition

qSOFA: also known as Quick SOFA, is defined by three criteria derived from three major organs used in the original SOFA score as acute respiratory failure defined by an increased respiratory rate superior to 22 bpm, altered cognition with a GCS<15 and a low blood pressure as a systolic blood pressure less than 100mmHg (Singer M. 2016). Contrarily to the SOFA score, the qSOFA is mortality predictor and not per se a standalone diagnostic test for sepsis.

II.2.2. Parameters of qSOFA scores

Altered mental status (GCS <15)

Respiratory rate ≥22

Systolic blood pressure < 100mmHg.

Each component of qSOFA score has either zero or 1 point, meaning that the minimum score is 0/3 and 3/3 for the maximum.

II.2.3. Interpretation of qSOFA score.

A “positive” qSOFA score (≥2) suggests high risk of poor outcome in patients with suspected infection. These patients should be more thoroughly assessed for evidence of organ dysfunction.

A positive qSOFA score by itself should not trigger sepsis-directed interventions like initiation of broad-spectrum antibiotics; rather it should prompt clinicians to further investigate for presence of organ dysfunction or to increase frequency of monitoring.

The sepsis-3 task force recommends that a positive qSOFA score should prompt the calculation of a SOFA score to confirm the diagnosis of sepsis. This remains controversial, as qSOFA has been shown to be more predictive than SOFA outside of the ICU setting.
Even if the qSOFA score is initially "negative" (<2), it can be repeated if there is a change in the patient's clinical status.

II.3. Empirical literature review

The quick SOFA score was introduced in February 2016 by the task force as a rapid bedside clinical score to identify patients with suspected infection that are at greater risk of bad outcome. The primary outcome was in-hospital mortality, and the second one was ICU length of stay greater or equal to three days. It was meant to replace the SIRS criteria that were believed to be less sensitive and specific (13). The qSOFA score was retrospectively derived and internally validated in a 2016 study by Seymour et al. 148,907 cases with suspected infection in and outside the ICU setting were included. In patients outside of the ICU with a qSOFA score ≥ 2, there was a 3- to 14-fold increase in the rate of in-hospital mortality. Among ICU patients, however, the predictive validity of SOFA for in-hospital mortality was statistically greater than qSOFA(14). The qSOFA score was prospectively validated in an emergency department population in a study including 879 participants across 30 emergency departments in four countries. The qSOFA score resulted in greater prognostic accuracy for in-hospital mortality than SIRS or severe sepsis(15).

Raith et al. externally validated the SOFA and qSOFA in a population of 184,875 participants with an infection-related admission diagnosis who were retrospectively identified and analyzed. An increase in SOFA score of 2 or more points had greater prognostic accuracy for in-hospital mortality than the SIRS criteria or qSOFA score in an ICU population(14).

In LMIC, other studies found mixed results in using the qSOFA score as a predictor of mortality. A prospective observational study of emergency department qSOFA scores at a single-center in Malawi found poor sensitivity when using the qSOFA score as designed, but noted a significant improvement when using GCS as independent risk factor for mortality (72% to 79%). In this example, the high-risk group consisted of those with a qSOFA score ≥2 and/or a GCS <15(16).

ALUSIA et al 2018 found that positive qSOFA scores had a sensitivity of 0.51 and a specificity of 0.83 for in-hospital mortality as compared with a sensitivity of 0.86 and a specificity of 0.29 for positive SIRS scores(17).

RUDAKEMWA at al. assessed the accuracy of the MEOWS and the qSOFA score in predicting mortality for obstetric patients admitted to ICU and found as easy tools as their components are part of routine clinical evaluation. They stated that qSOFA and MEOWS have good discriminative power with an AUROC of 0.76 [0.65-0.87], $p < 0.0001$ and 0.77 [0.66-0.880], $p < 0.0001$ respectively(18).

CHAPTER III. METHODOLOGY

III.1. Introduction

This study is a mixed retrospective and prospective cohort study performed among adult ICU patients at CHUK, the largest referral hospital in Rwanda with 519 beds, including, 7 ICU beds and 4 HDU (High Dependency Unit) beds. After obtaining approvals from the Institutional Review Board (IRB) of the University of Rwanda and from the hospital, this study was conducted during 20 months from May 2019 to December 2020. Participants of this study were all adult patients who were above 18 years old and admitted to the ICU or HDU during the period of the study. The researcher excluded patients who were intubated or sedated prior to ICU admission, or who were suffered from cardiac arrest before ICU admission. Census sampling method was used and target sample size was calculated using Epi Info version 3 (US Centers for Disease Control, Atlanta, GA) considering that the ICU/CHUK admits 500 patients per year and then analyzed using a combination of SPSS and Excel software.

III.2. Research design

Mixed retrospective and prospective cohort study was conducted during 20 months from May 2019 to December 2020.

III.3. Research approach

Quantitative approach was applied to the present research. A quantitative approach is the study that involves statistical measurement (numbers) or numerical analysis of data(19).

III.4. Research Setting

The study was conducted at Kigali University Teaching Hospital (CHUK). This was built in 1918 by a group of missionaries referred to as Pennies through the initiative of the official Authorities of Belgium. The hospital began with four rooms for hospitalization and a dispensary. CHUK was awarded the status of a referral and teaching hospital on 7/12/2000 by the law N^{o}41/2000 and then expanded. Currently CHUK has a capacity of admitting 519 patients. Its mission is to provide education and clinical training for medical profession, to deliver high-

quality medical care for all categories of people and to develop research. The intensive care unit at CHUK is made of 7 ICU beds and 4 HDU beds.

III.5. Study population

The study had 148 participants including 62 participants for retrospective and 86 participants for prospective study.

III.6. Sampling.

III.6.1. Sampling strategy.

In this index study a census sampling method was used. Census sampling is a strategy of sampling during which everyone in the research population is part of the sample, and the whole research population make the research sample size.

Inclusion criteria

All patients who were above 18 years old admitted in ICU and HDU during the period of the study.

Exclusion criteria

Intubation; sedation or cardiac arrest prior to ICU admission.

Refusal of patient or caretaker to participate in the research.

III.6.2. Sample size.

In our research, the target sample size was made by all patients fulfilling the inclusion criteria. Thus the total sample size was 148 participants made by 62 cases for retrospective and 86 cases for prospective study.

III.7. Data collection

III.7.1. Data collection tool.

To achieve the objectives of our research, an elaborate a tool composed by 6 parts including hospital and demographic data; patient's service origin; indication of ICU admission; qSOFA parameters; patient's comorbidities and finally ICU outcomes.

Validity of the tool.

The validity was ensured by expert in critical care and current evidence based practice.

Reliability of the tool.

The reliability was ensured by calculating internal consistency reliability coefficient of 0.85 (Cronbach Alpha) and test retest method which showed a reliability coefficient of 0.83, p=0.04.

III.7.2. Data collection procedure

The collection of data comprised a retrospective cohort collected from ICU registries, files and the open clinic system from May 2019 to February 2020. From March to December 2020, we collected data for the prospective cohort and we recorded desired data within one hour after admission in ICU and or HDU. A pre-designed questionnaire composed by 6 parts including hospital and demographic data; patient's service origin; indication of ICU admission; qSOFA parameters; patient's comorbidities and finally ICU outcomes have been used to collect data.

III.8. Data entry and statistical analysis

Data were entered in Epi-Info version 3 then analyzed using a combination of SPSS and Excel software. We defined high versus low-risk groups according to their qSOFA scores, and those with a score greater than or equal to 2 points were defined as high-risk group and the ones with less than 2 points of qSOFA score were qualified as low-risk group. Based on this classification, we calculated raw mortality and prognostic performance values for both risk groups and analyzed AUROC as primary outcome and average ICU length of stay and post- ICU discharge mortality rate as secondary outcome as well as sensitivity, specificity and positive / negative predictive value. We also compared the age groups with Wilcoxon test.

III.9. Ethical considerations

III.9.1. Ethical issues:

I obtained an ethical approval N° 571/CMHS IRB/2019 from the IRB of the University of Rwanda, College of Medicine and Health Sciences.

I obtained also the ethical approval from the University Teaching Hospital of Kigali to conduct this data collection in its ICU and archive.

III.10. Data Management

Multiple measures were taken to ensure the confidentiality such as electronic password-protected documents. Hard copies have to be kept for 5 years in locked file and after this time they will be discarded. Only the principal investigator has the access to these data.

III.11. Data dissemination

Research findings will be presented to the ICU team and all ICU users in CHUK.

I will present results in local conferences where hospital and national decision makers may be present.

Finally, I will write and publish a paper in local medical journals as well as in international peer review journal for further research consultation.

III.12.Problems and Limitations of the Study

The study was in part retrospective, with important consequences such as missing data and lack of uniformity in the assessment of qSOFA (particularly in the GCS assessment). However, only 4.72% of participants were excluded due to a lack of more than one qSOFA parameter. The study was limited to adult ICU patients and was only performed as simple observational study at one hospital centre. This study did not test whether the qSOFA score reflects any information that might discriminate different types of infection or infection-associated organ dysfunction in the assessment of outcomes.

CHAPTER IV. RESULTS

IV.1. Introduction

This chapter presents the findings of our study according to the research objectives. The results are presented in tables with percentages based on the total high or low-risk group not on the number of values present and figures according to qSOFA risk categories which are preceded by a short summary of the contents within the tables or figures.

IV.2. Patient's enrolment

The study consisted of 148 participants. During the data collection period, we excluded all cases that did not meet our inclusion criteria. During data analysis, we exclude cases where less than 2 variables contributing to the qSOFA score were available, a total of 7 participants. There were 40 participants in the high-risk group (with a qSOFA score ≥2) and 101 participants in the low-risk group.

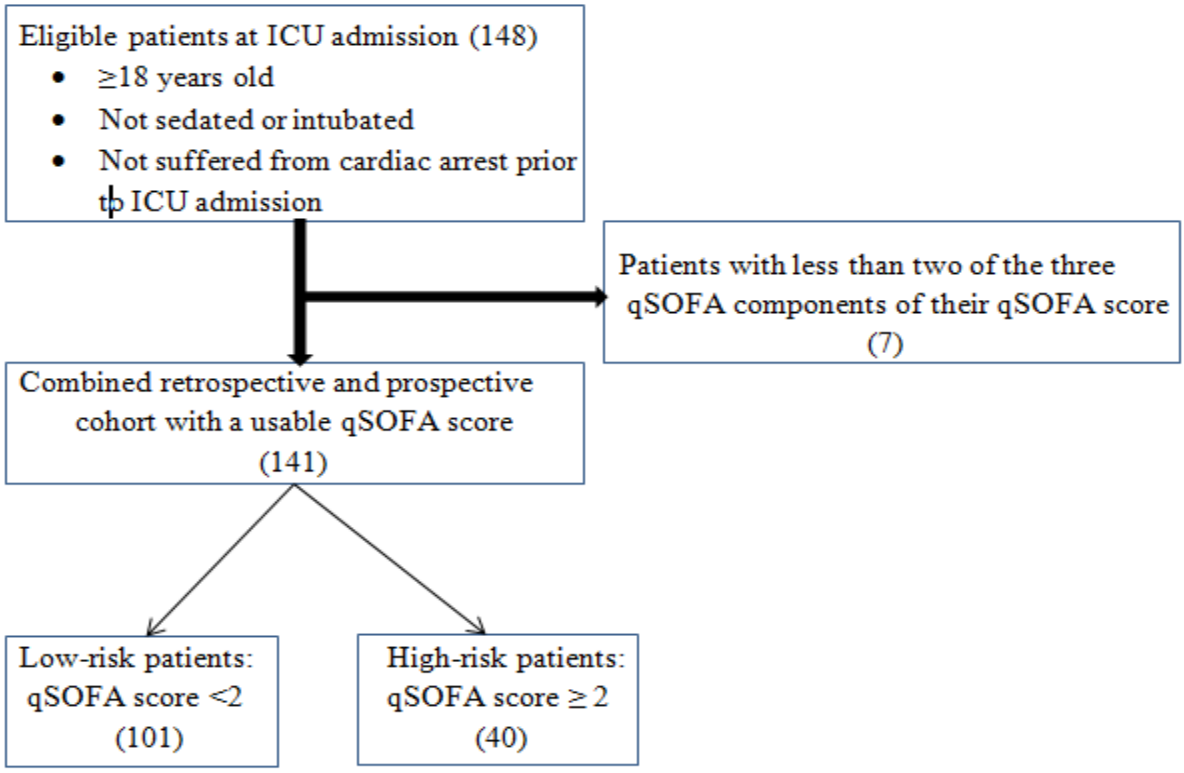

Figure 1 Participant inclusion flow chart.

IV.3. Patient's characteristics at ICU admission.

A hundred forty one patients were enrolled including 23 vs. 52 females and 17 vs. 49 males in high-risk vs. low-risk group respectively. Twenty-three participants had a qSOFA score of 0; 78 had a score of 1; 36 had a score of 2, and 4 had a score of 3. The median age was 33 (IQR: 24-41.5) for the high-risk group, which was significantly smaller than the median age of 40 (IQR: 31-59) for the low-risk group ($Z=2.55$, $p<0.05$).

Table 1 Patient's characteristics

Characteristics	High-risk	Low-risk	Wilcoxon Test	P-value
Total (%)	40 (28.4)	101 (71.6)		
Gender, No. (%)				
Male	17 (42.5)	49 (48.5)		
Female	23 (57.5)	52 (51.5)		
Age, (years)				
Median (IQR)	33 (24-41.5)	40 (31-59)	Z=2.55	<0.05
No. (%)				
<75	37 (92.5)	87 (86.1)		
≥75	3 (7.5)	14 (13.9)		

IV.4. Reason of ICU admission.

As anticipated in the high-risk group, I found a significantly higher proportion of cases with altered mental status (75%), respiratory failure or distress (75%), confirmed sepsis (40%) and hypotensive shock (35%) as the admitting diagnosis.

Table 2 Admitting diagnosis.

Admitting diagnosis	High-risk	Low-risk	P-value
Altered Mental Status, No. (%)	30 (75)	42 (41.6)	< 0.00001
Trauma, No. (%)	7 (18)	25 (25)	
Status epilepticus, No. (%)	1 (3)	3 (3)	

Respiratory failure or distress, No. (%)	30 (75)	31 (30)	< 0.00001
Acute renal failure, No. (%)	1 (2.5)	5 (5)	
Intoxication, No. (%)	0	2 (2)	
Hypotensive shock, No. (%)	14 (35)	4 (4)	< 0.00001
Post-operative recovery, No. (%)	3 (7.5)	29 (28.7)	0.00023
Pre-eclampsia and/or eclampsia, No. (%)	1 (2.5)	3 (3)	
Confirmed sepsis, No. (%)	16 (40)	14 (14)	< 0.00001

IV.5. qSOFA parameters.

There were 32 (80%) participants with GCS <15 in the high-risk group and 40 (39.6%) in the low-risk group. The median respiratory rate was 27 breaths per minute (IQR: 24-33) for high-risk group and 20 breaths per minute (IQR: 17-26) for the low-risk group. The median systolic blood pressure was 108 mmHg (IQR: 90-142) for the high-risk group and 127 mmHg (IQR: 110-139) for the low-risk group.

Table 3 qSOFA parameters.

qSOFA parameters	High-risk	Low-risk
Glasgow Coma Scale score <15, No. (%)[a]	32 (80)	40 (39.6)
Respiratory rate, median (IQR), breaths/min	27 (24-33)	20 (17-26)
Systolic Blood pressure, median (IQR), mmHg	108 (90-142)	127 (110-139)
[a] percentage are based on the total high or low-risk group not on the number of values present		

IV.6. Patients comorbidities

In this study, 55% in high-risk and 53% in low-risk group were not presenting any comorbidity. However, I found a significantly higher number of patients with AKI or CKD in the high-risk group (12.5%) than in the low-risk group (5%).

Table 4 Comorbidities.

Comorbidities, No. (%)	High-risk	Low-risk	P-value
Diabetes mellitus, No. (%)	7 (17.5)	11 (10.9)	
Cardio-vascular disease, No. (%)	8 (21)	24 (24)	
Cancer, No. (%)	0	2 (2)	
Chronic respiratory failure, No. (%)	1(3)	2 (2)	
Acute Kidney Injury or Chronic Kidney Disease, No. (%)	5 (12.5)	5 (5)	0.048
Chronic liver disease, No. (%)	3 (8)	2 (2)	
HIV or AIDS, No. (%)	3 (8)	7 (7)	
Other	4 (10)	11 (11)	
Non comorbities, No. (%)	22 (55)	54 (53.4)	

IV.7. ICU outcomes

The overall CHUK ICU mortality rate during the study period was 39.3% in 2019 and 40.1% in 2020. The ICU mortality rate in my sample was 20% in the high-risk and 19.6% in the low-risk groups. The post-ICU Mortality rates were 0% in the high-risk group vs 3.5% in the low-risk group. The median ICU length of stay was 6 days (IQR 2-10) for the high-risk group and 5 days (IQR 3-11) for the low-risk group with an absolute difference of 2.89 (95% CI -1.83 to 7.62, p-value 0.118).

Table 5. Primary and secondary outcomes organized into total patient cohort and qSOFA risk groups.

	Overall	High Risk	Low Risk	P-value
ICU Mortality Rate (%)	20.%	20.0%	19.6%	0.98
Post-ICU Mortality Rate (%)	4%	0%	4%	0.65
Length of Stay median (IQR)	5 (3-10)	6 (2-10)	5 (3-11)	0.12[a]

[a] p-value based on an absolute difference of 2.89

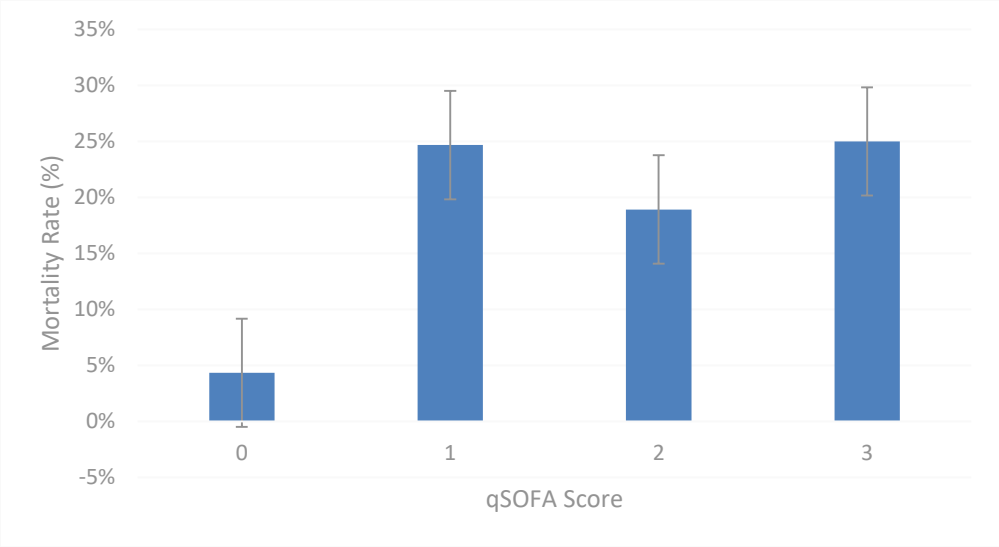

Figure 2. Mortality rates organized by qSOFA scores.

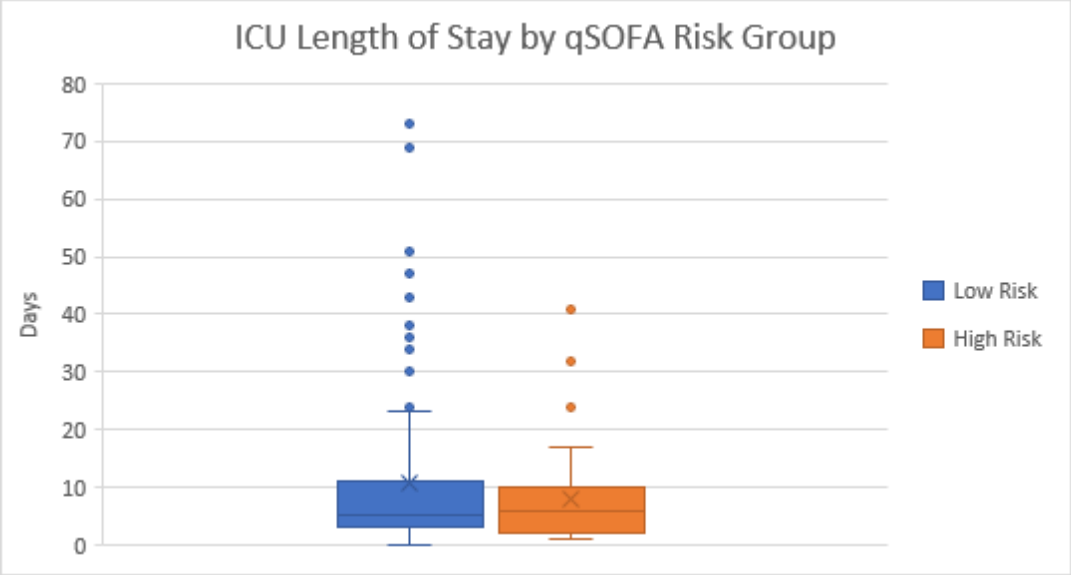

Figure 3. ICU length of stay outcomes organized by qSOFA risk groups

In our study, the prognostic performance value of the qSOFA score (with a cutoff of 2) in predicting ICU mortality was as follow: 29% sensitivity, 73% specificity, 21% PPV, and 80% NPV. The area under the curve was 0.555 (95% CI -.528-0.589).

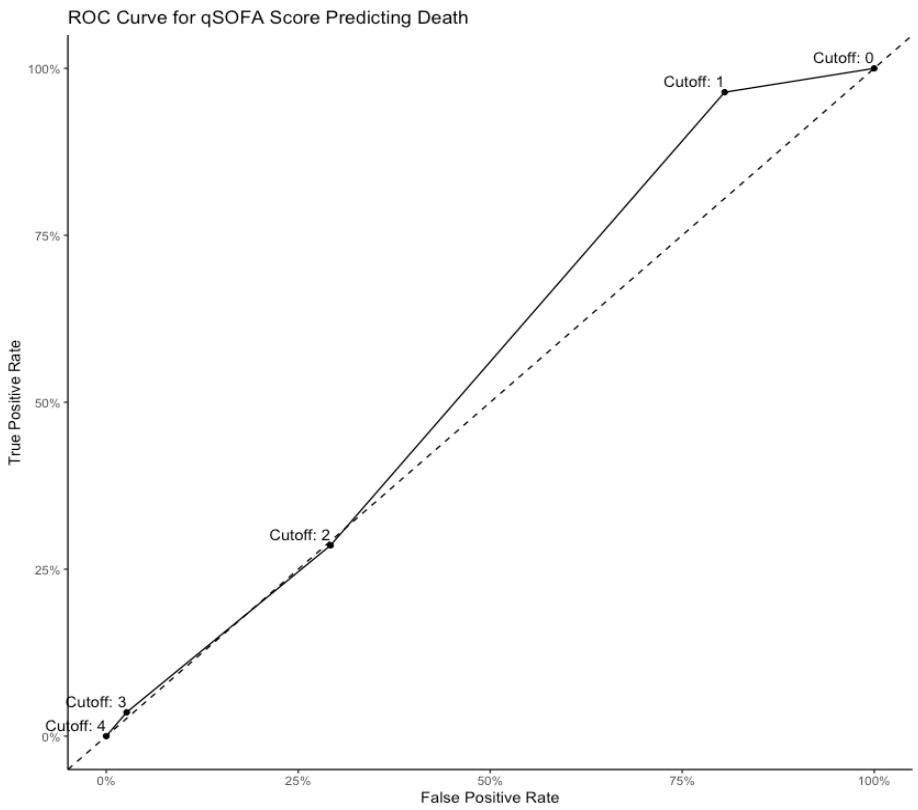

Figure 4 Receiver Operating Curve for ICU mortality: 0.555 (95% CI 0.528 - 0.589)

The performance values of the qSOFA in predicting post-ICU mortality were 72% specificity and 95% NPV.

CHAPTER IV. DISCUSSION

This combined retrospective and prospective study had the main objective of determining the impact of qSOFA score at admission to ICU in predicting hospital outcomes for critically ill patients at CHUK and found the qSOFA score to be a poor predictor of ICU mortality at this single center. The overall ICU mortality rate in my cohort was 20% which was half of the overall ICU mortality during the timeframe of the study. There was no significant difference in crude mortality between high-risk and low-risk groups as defined by qSOFA (p-value 0.98), indicating a qSOFA score of two or greater was not associated with a higher mortality. For ICU mortality, we found a sensitivity of 29%, a specificity of 73%, a positive predictive value of 21%, and a negative predictive value of 80%. These predictive performance values show that the qSOFA score performed better at ruling out mortality, but not reliably. With an AUROC of 0.555, I found that a qSOFA score of 0 is a reliable predictor of survival but that scoring a qSOFA score of 1 or above is not. For the secondary outcome, the qSOFA score also did not serve as an accurate predictor of post-ICU mortality (p-value 0.07). For this outcome, the specificity was 71% and the negative predictive value was 95%, again indicating that the qSOFA could potentially be more useful at ruling out mortality risk in those with a low qSOFA score. Another secondary outcome for this study was ICU length of stay. I did not find a significant difference in the length of stays between the two risk groups.

In this study, the qSOFA score at ICU admission showed 29% sensitivity with a cutoff of 2 and a specificity of 73%. Our findings are supported by a single center retrospective study out of the United States that found the sensitivity and specificity for qSOFA in the unadjusted model to be 34.8% and 76.1%, with no statistically significant difference between those who did and did not have a qSOFA of 2 or more at ICU admission. Two studies out of similar high-income countries that looked to validate the qSOFA score outside the ICU setting using prospective methods also supported my findings with relatively low sensitivities of 63% and 29.7% for qSOFA scores ≥2 in predicting mortality among septic patients. Note that, a high specificity (66.7% and 91.3% respectively) was found, which mirrors the specificity of 73% in my study (20,21).

My findings do agree with some of the literature surrounding the use of the qSOFA score in LMIC and globally, which varies greatly. A global meta-analysis from 2018 found that the

qSOFA score was a poorly sensitive predictor of ICU mortality than the SIRS criteria, but was more specific (22). One explanation the authors proposed for this was the heterogeneity of average ages within their included studies. Looking at age as a possible explanation for poor performance, my study provides useful input as the average age of 43 differs greatly from similar studies that validated the qSOFA which typically report median or average ages in the mid-60s (14,15).

When looking specifically at LMIC, our findings are different from research in Malawi and Gabon that reported sensitivity and specificity values for overall hospital mortality of 72% and 68% vs 87% and 75%, respectively (16,17,23). Other studies have also had mixed results in using the qSOFA score as a predictor of mortality. A prospective observational investigation of emergency department qSOFA scores at a single-center in Malawi found poor sensitivity when using the qSOFA score as designed, but noted a significant improvement when using GCS as independent risk factor for mortality (72% to 79%). In this example, the high-risk group consisted of those with a qSOFA score ≥2 and/or a GCS <15 (23). When applying this model to my cohort, I had a markedly larger number in the high-risk group but still no significant difference in crude mortality and a consistent mortality rate for both groups. I did however find an increase in the specificity from 29% to 57%, but a decrease in the specificity from 72% to 43%, indicating that the Huson et al 2017 model did not enhance the utility of the qSOFA score as a predictor of ICU mortality in our population.

In this study, it is notable that the overall ICU mortality for this time period was remarkably different from that of the participating cohort (40% overall, 20% participating). This raises questions about the types of patients that were included in the study and how the exclusion criteria influenced the mortality within our cohort. For example, patients that came to the ICU already intubated, sedated or post cardiac arrest that were mostly on mechanical ventilators were excluded from this study. The literature shows that the mortality rate of ventilatory support in low-resource countries varies from 30-70% (24–26). Excluding ventilated patients alters the predictive ability of the qSOFA score for these ICUs as it is possible that much of the mortality is happening in this population.

These findings may have important clinical implications. Even though the qSOFA score is widely accepted as a tool of identification and predictor of mortality of septic patients, it failed

to predict mortality and ICU length of stay in each individual group of patients in this study and in other studies in LMICs (9,10,27). Thus, clinicians specifically in ICU and researchers now have data to support the idea for seeking another rapid clinical decision-making tool to be tested among ICU patients in LMICs.

CHAPTER VI. CONCLUSION and RECOMMENDATION

I reported the retrospective and prospective data on the impact of qSOFA in terms of predicting ICU patients' mortality and length of stay in a resource-limited setting and found that the qSOFA score is a poor predictor of outcome in this environment.

I recommend further research in a bigger context by improving clinical assessment of qSOFA, by working in many centres to increase the sample size and awareness on qSOFA utilization.

REFERENCES

1. Martin GS, Mannino DM, Eaton S, Moss M. The Epidemiology of Sepsis in the United States from 1979 through 2000. N Engl J Med. 2003 Apr 17;348(16):1546–1554.

2. Fleischmann C, Scherag A, Adhikari NKJ, Hartog CS, Tsaganos T, Schlattmann P, et al. Assessment of Global Incidence and Mortality of Hospital-treated Sepsis. Current Estimates and Limitations. Am J Respir Crit Care Med. 2016 Feb;193(3):259–272.

3. Vincent J-L, Marshall JC, Ñamendys-Silva SA, François B, Martin-Loeches I, Lipman J, et al. Assessment of the worldwide burden of critical illness: the Intensive Care Over Nations (ICON) audit. The Lancet Respiratory Medicine. 2014 May;2(5):380–386.

4. Sakr Y, Jaschinski U, Wittebole X, Szakmany T, Lipman J, Ñamendys-Silva SA, et al. Sepsis in Intensive Care Unit Patients: Worldwide Data From the Intensive Care over Nations Audit. Open Forum Infectious Diseases [Internet]. 2018 Dec 1 [cited 2019 Oct 22];5(12). Available from: https://academic.oup.com/ofid/article/doi/10.1093/ofid/ofy313/5193171

5. Sugira V, Simpao M, Ogbuagu O, Walker T. Predictors of Mortality From Sepsis Smong an African Patient Cohort: A Prospective Study From Two Tertiary Healthcare Facilities in Kigali, Rwanda. Open Forum Infect Dis. 2015; *2, 821,* https://doi.org/10.1093/ofid/ofv133.538

6. Murthy S, Leligdowicz A, Adhikari N. Intensive Care Unit Capacity in Low-Income Countries: A Systematic Review. PLOS ONE. 2015 Jan 24;10:e0116949.

7. Levy MM, Evans LE, Rhodes A. The Surviving Sepsis Campaign Bundle: 2018 update. Intensive Care Med. 2018 Jun;44(6):925–928.

8. Kaukonen K-M, Bailey M, Pilcher D, Cooper DJ, Bellomo R. Systemic Inflammatory Response Syndrome Criteria in Defining Severe Sepsis. N Engl J Med. 2015 Apr 23;372(17):1629–1638.

9. Minejima E, Delayo V, Lou M, Ny P, Nieberg P, She RC, et al. Utility of qSOFA score in identifying patients at risk for poor outcome in Staphylococcus aureus bacteremia. BMC Infect Dis. 2019 Dec;19(1):149. doi: 10.1186/s12879-019-3770-4

10. Rudd KE, Seymour CW, Aluisio AR, Augustin ME, Bagenda DS, Beane A, et al. Association of the Quick Sequential (Sepsis-Related) Organ Failure Assessment (qSOFA) Score With Excess Hospital Mortality in Adults With Suspected Infection in Low- and Middle-Income Countries. JAMA. 2018 05;319(21):2202–2211.

11. Nkundimana G. COLLEGE OF MEDICINE AND HEALTH SCIENCES. :42.

12. Marshall JC, Bosco L, Adhikari NK, Connolly B, Diaz JV, Dorman T, et al. What is an intensive care unit? A report of the task force of the World Federation of Societies of Intensive and Critical Care Medicine. Journal of Critical Care. 2017 Feb;37:270–276.

13. Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA. 2016 Feb 23;315(8):801-810.

14. Raith EP, Udy AA, Bailey M, McGloughlin S, MacIsaac C, Bellomo R, et al. Prognostic Accuracy of the SOFA Score, SIRS Criteria, and qSOFA Score for In-Hospital Mortality Among Adults With Suspected Infection Admitted to the Intensive Care Unit. JAMA. 2017 Jan 17;317(3):290-300.

15. Freund Y, Lemachatti N, Krastinova E, Van Laer M, Claessens Y-E, Avondo A, et al. Prognostic Accuracy of Sepsis-3 Criteria for In-Hospital Mortality Among Patients With Suspected Infection Presenting to the Emergency Department. JAMA. 2017 Jan 17;317(3):301-308.

16. Huson MAM, Kalkman R, Grobusch MP, van der Poll T. Predictive value of the qSOFA score in patients with suspected infection in a resource limited setting in Gabon. Travel Medicine and Infectious Disease. 2017 Jan;15:76–77.

17. Aluisio AR, Garbern S, Wiskel T, Mutabazi ZA, Umuhire O, Ch'ng CC, et al. Mortality outcomes based on ED qSOFA score and HIV status in a developing low income country. The American Journal of Emergency Medicine. 2018 Nov;36(11):2010–2019.

18. Rudakemwa A, Cassidy AL, Twagirumugabe T. High Mortality Rate of Obstetric Critically ILL Patients in Rwanda and Its Predictability [Internet]. In Review; 2020 May [cited 2021 May 27]. Available from: https://www.researchsquare.com/article/rs-29207/v1

19. Slevitch L. Qualitative and Quantitative Methodologies Compared: Ontological and Epistemological Perspectives. Journal of Quality Assurance in Hospitality & Tourism. 2011 Feb;12(1):73–81.

20. Churpek MM, Snyder A, Han X, Sokol S, Pettit N, Howell MD, et al. Quick Sepsis-related Organ Failure Assessment, Systemic Inflammatory Response Syndrome, and Early Warning Scores for Detecting Clinical Deterioration in Infected Patients outside the Intensive Care Unit. Am J Respir Crit Care Med. 2017 Apr;195(7):906–911.

21. Williams JM, Greenslade JH, McKenzie JV, Chu K, Brown AFT, Lipman J. Systemic Inflammatory Response Syndrome, Quick Sequential Organ Function Assessment, and Organ Dysfunction. Chest. 2017 Mar;151(3):586–596.

22. Maitra S, Som A, Bhattacharjee S. Accuracy of quick Sequential Organ Failure Assessment (qSOFA) score and systemic inflammatory response syndrome (SIRS) criteria for predicting mortality in hospitalized patients with suspected infection: a meta-analysis of observational studies. Clinical Microbiology and Infection. 2018 Nov;24(11):1123–1129.

23. Huson MAM, Katete C, Chunda L, Ngoma J, Wallrauch C, Heller T, et al. Application of the qSOFA score to predict mortality in patients with suspected infection in a resource-limited setting in Malawi. Infection. 2017 Dec;45(6):893–896.

24. Franca SA, Toufen C, Hovnanian ALD, Albuquerque ALP, Borges ER, Pizzo VRP, et al. The epidemiology of acute respiratory failure in hospitalized patients: A Brazilian prospective cohort study. Journal of Critical Care. 2011 Jun;26(3):330.e1-330.e8.

25. Khatib KI, Dixit SB, Joshi MM. Factors determining outcomes in adult patient undergoing mechanical ventilation: A “real-world” retrospective study in an Indian Intensive Care Unit. Int J Crit Illn Inj Sci. 2018 Mar;8(1):9–16.

26. Prin M, Itaye T, Clark S, Fernando RJ, Namboya F, Pollach G, et al. Critical Care in a Tertiary Hospital in Malawi. World J Surg. 2016 Nov;40(11):2635–2642.

27. Canet E, Taylor DM, Khor R, Krishnan V, Bellomo R. qSOFA as predictor of mortality and prolonged ICU admission in Emergency Department patients with suspected infection. Journal of Critical Care. 2018 Dec;48:118–123.

ANNEXES

The IRB approval from University of Rwanda-CMHS and CHUK.

UNIVERSITY of RWANDA

COLLEGE OF MEDICINE AND HEALTH SCIENCES

DIRECTORATE OF RESEARCH & INNOVATION

CMHS INSTITUTIONAL REVIEW BOARD (IRB)

Kigali, 23rd/December/2019

Dr Remy Steve MBAHIRE
School of Medicine and Pharmacy, CMHS, UR

Approval Notice: No 571/CMHS IRB/2019

Your Project Title ***"Impact of the "quick Sequential Organ Failure Assessment" QSOFA at admission to the intensive care unit on hospital outcome for critically ill patient at Kigali University Teaching Hospital"*** has been evaluated by CMHS Institutional Review Board.

		Involved in the decision		
			No (Reason)	
Name of Members	**Institute**	Yes	**Absent**	**Withdrawn from the proceeding**
Prof Kato J. Njunwa	UR-CMHS		X	
Prof Jean Bosco Gahutu	UR-CMHS	X		
Dr Brenda Asiimwe-Kateera	UR-CMHS	X		
Prof Ntaganira Joseph	UR-CMHS	X		
Dr Tumusiime K. David	UR-CMHS	X		
Dr Kayonga N. Egide	UR-CMHS	X		
Mr Kanyoni Maurice	UR-CMHS		X	
Prof Munyanshongore Cyprien	UR-CMHS	X		
Mrs Ruzindana Landrine	Kicukiro district		X	
Dr Gishoma Darius	UR-CMHS	X		
Dr Donatilla Mukamana	UR-CMHS	X		
Prof Kyamanywa Patrick	UR-CMHS		X	
Prof Condo Umutesi Jeannine	UR-CMHS		X	
Dr Nyirazinyoye Laetitia	UR-CMHS	X		
Dr Nkeramihigo Emmanuel	UR-CMHS		X	
Sr Maliboli Marie Josee	CHUK	X		
Dr Mudenge Charles	Centre Psycho-Social	X		

After reviewing your protocol during the IRB meeting of where quorum was met and revisions made on the advice of the CMHS IRB submitted on 23rd December 2019, **Approval has been granted to your study.**
Please note that approval of the protocol and consent form is valid for **12 months**.

Email: researchcenter@ur.ac.rw P.O Box 3286 Kigali, Rwanda www.ur.ac.rw

You are responsible for fulfilling the following requirements:

1. Changes, amendments, and addenda to the protocol or consent form must be submitted to the committee for review and approval, prior to activation of the changes.
2. Only approved consent forms are to be used in the enrolment of participants.
3. All consent forms signed by subjects should be retained on file. The IRB may conduct audits of all study records, and consent documentation may be part of such audits.
4. A continuing review application must be submitted to the IRB in a timely fashion and before expiry of this approval
5. Failure to submit a continuing review application will result in termination of the study
6. Notify the IRB committee once the study is finished

Sincerely,

Date of Approval: The 23rd December 2019

Expiration date: The 23rd December 2020

Professor GAHUTU Jean Bosco
Chairperson Institutional Review Board,
College of Medicine and Health Sciences, UR

Cc:

- Principal College of Medicine and Health Sciences, UR
- University Director of Research and Postgraduate Studies, UR

CENTRE HOSPITALIER UNIVERSITAIRE
UNIVERSITY TEACHING HOSPITAL

Quality Health Care
Training & Research

Ethics Committee / Comité d'éthique

17,Jan,2020 *Ref.:EC/CHUK/004/2020*

Review Approval Notice

Dear Remy Steve MBAHIRE,

Your research project: ***"IMPACT OF "quick SEQUENTIAL ORGAN FAILURE ASSESSMENT" qSOFA AT ADMISSION TO THE INTENSIVE CARE UNIT ON HOSPITAL OUTCOME FOR CRITICALLY ILL PATIENT AT KIGALI UNIVERSITY TEACHING HOSPITAL. "***

During the meeting of the Ethics Committee of University Teaching Hospital of Kigali (CHUK) that was held on 17,Jan,2020 to evaluate your request for ethical approval of the above mentioned research project, we are pleased to inform you that the Ethics Committee/CHUK has approved your research project.

You are required to present the results of your study to CHUK Ethics Committee before publication by using this link:www.chuk.rw/research/fullreport/?appid=30&&chuk.

PS: Please note that the present approval is valid for 12 months.

Yours sincerely,

Dr Emmanuel Rusingiza Kamanzi
The Chairperson, Ethics Committee,
University Teaching Hospital of Kigali

ETHICS COMMITTEE
CHUK

Scan code to verify.

" University teaching hospital of Kigali Ethics committee operates according to standard operating procedures (Sops) which are updated on an annual basis and in compliance with GCP and Ethics guidelines and regulations "

DATA COLLECTION FORM

Hospital and demographic data

Patient identification number

Gender

Date of birth Age

Hospital admission date

ICU admission date

Patient origin

- ☐ Emergency Department
- ☐ Operating Room
- ☐ Post Anesthesia Care Unit
- ☐ Maternity service
- ☐ Surgical ward
- ☐ Medical ward
- ☐ Out of CHUK

Indication of ICU admission

- ☐ Altered mental status
- ☐ Renal failure
- ☐ Respiratory distress / failure
- ☐ Hypotension / shock
- ☐ Polytrauma
- ☐ Severe pre-eclampsia / eclampsia
- ☐ Infection
- ☐ Post-operative recovery

☐ Status epilepticus

☐ Intoxication

☐ Others (specify)

qSOFA parameters (during one hour of ICU admission**)**

GCS		☐ GCS unavailable
RR		☐ RR unavailable
SBP		☐ SBP unavailable

Patient comorbidities

☐ Diabetes mellitus	☐ AKI / CKD
☐ Chronic respiratory failure	☐ HIV/AIDS
☐ Chronic liver diseases	☐ Cancer
☐ Cardiovascular diseases (specify)	
☐ No comorbidity	

ICU outcome

ICU discharge date		☐ Died in ICU
Hospital discharge date		☐ Died in Hospital
ICU length of stay		