ORIGINAL ARTICLE

Value of Shock Index in Prognosticating The Short Term Outcome of Death for Patients Presenting With Severe Sepsis and Septic Shock in The Emergency Department

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SUMMARY

Introduction: The importance of early recognition and treatment of sepsis and its effects on short-term survival outcome have long been recognized. Having reliable indicators and markers that would help prognosticate the survival of these patients is invaluable and would subsequently assist in the course of effective dynamic triaging and goal directed management.

Study Objectives: To determine the prognosticative value of Shock Index (SI), taken upon arrival to the emergency department and after 2 hours of resuscitation on the short-term outcome of severe sepsis and septic shock patients.

Methodology: This is a retrospective observational study involving 50 patients admitted to the University of Malaya Medical Centre between June 2009 and June 2010 who have been diagnosed with either severe sepsis or septic shock. Patients were identified retrospectively from the details recorded in the registration book of the resuscitation room. 50 patients were selected for this pilot study. The population comprised 19 males (38%) and 31 females (62%). The median (min, max) age was 54.5 (17.0, 84.0) years. The number of severe sepsis and septic shock cases were 31 (62%), and 19 (38%) respectively. There were 17 (34%) cases of pneumonias, 13 (26%) cases of urological sepsis, 8 (16%) cases of gastro intestinal tract related infections and 12 (24%) cases of other infections. There were a total of 23 (46%) survivors and 27 (54%) deaths. The value of the shock index is defined as systolic blood pressure divided by heart rate was calculated. Shock Index on presentation to ED (SI 1) and after 2 hours of resuscitation in the ED (SI 2). The median, minimum and maximum variables were tested using Mann-Whitney U and Chi square analysis. The significant parameters were re-evaluated for sensitivity, specificity and cut-off points. ROC curves and AUC values were generated among these variables to assess prognostic utility for outcome.

Results: Amongst all 7 variables tested, 2 were tested to be significant (p: < 0.05). From the sensitivity, specificity and ROC analysis, the best predictor for death was (SI 2) with a sensitivity of 80.8%, specificity of 79.2%, AUC value of 0.8894 [CI95 0.8052, 0.9736] at a cut-off point of ≥1.0.

Conclusion: (SI 2) may potentially be utilized as a reliable predictor for death in patients presenting with septic shock and severe sepsis in an emergency department. This parameters should be further analyzed in a larger scale prospective study to determine its validity.

INTRODUCTION

The importance of early recognition and treatment of sepsis and its effects on short-term survival outcome have long been recognized. Having reliable indicators and markers that would help prognosticate the survival of these patients is invaluable and would subsequently assist in the course of effective dynamic triaging and goal directed management[1].

Sepsis is a major cause of mortality and morbidity throughout the world. Additionally, the personal and economic costs of treatment are high. It is a complex syndrome that is difficult to define, diagnose and treat. It produces a range of clinical conditions caused by the body's systemic response to an infection, which causes rapid deterioration into severe sepsis. This in turn, accompanied by single or multiple organ dysfunction or failure, often leads to death if poorly treated or recognized.

The management of sepsis is closely related to the availability of relevant equipment and efficacy of clinical and serological indices, which is used as a guide for the prognostication and effective treatment goals. The development of cost effective and easily attainable clinical parameters that would effectively prognosticate the outcome of sepsis patients would be invaluable within an emergency department setting. Availability of such parameters would result in optimized triaging, risk stratification and also contribute to accurate identification of intensive care unit candidates amongst severely ill patients, at a fraction of the cost.

Data indicates, in 2001 the annual incidence of sepsis is over 18 million cases worldwide. The number of sepsis patients is projected to increase by 1.5% per annum, indicating by the year 2020 there will be an additional 1 million sepsis cases per year in the USA alone[2]. This high incidence of sepsis cases would critically raise the burden on personal and healthcare resources. Sepsis ranks as the 10th leading cause

of death in America and kills approximately 1,400 people worldwide every day [3,4]. In 2002, sepsis was the 3rd highest contributor to death by all cause in Malaysia, mainly attributed by lower respiratory tract infections [5]. A precise number of sepsis related mortalities is difficult to estimate as the cause of death on patients' death certificates is commonly attributed to related co-morbidities rather than sepsis itself, resulting in almost half of deaths left unattributed to sepsis [2,4].

The financial cost of treating sepsis is exorbitant and continuously escalating especially in the face of the pro-inflation global economy. It imposes a burden to many developing countries and even amongst developed nations. In most countries, the intensivist, pulmonologist, critical care physician and the ICU anesthetist lead the management of sepsis. However, many other healthcare professionals provide consultation for and support to sepsis cases, including emergency physicians, infectious disease physicians, surgeons, oncologists, hematologists, urologists, nephrologists, internal medicine physicians, family practitioners, pharmacists and nurses. The intensive demands upon hospital staff, equipments and facilities to treat sepsis patients places a significant burden on healthcare resources and accounts for 40% of total ICU expenditure [4].

In a published study the average cost of sepsis treatment in the United States was USD $22,100 per patient in the year 2002. In another related study the average treatment cost in the United Kingdom was USD $10,622 per patient in the year 1998[6]. In a similar study conducted in 2002, the average treatment cost for patients presenting with severe sepsis and septic shock at two health care institutions in Quebec, Canada was USD $11,474 per patient[7]. There is no published data on average cost expenditure per patient for the management of sepsis related illnesses in Malaysia.

Systemic Inflammatory Response Syndrome (SIRS) is a state of inflammation affecting the whole body, frequently a response of the immune system to infection, trauma, or any physiological stress. SIRS was first described by Dr. Nelson, of the University of Toronto, at the Nordic Micro Circulation meeting in Geilo, Norway in February of 1983. Criteria's for SIRS were established in 1992 as part of the American College of Chest Physicians and the Society of Critical Care Medicine Consensus Conference[4].

According to the International Sepsis Definitions Conference, sepsis is defined as the presence of infection in association with meeting SIRS criteria's[8]. Severe sepsis is defined as evidence of end-organ dysfunction such as altered mental status, episode of hypotension, elevated serum creatinine, tissue hypoperfusion manifested by a lactate level greater than 4 mg/dL or evidence of disseminated intravascular coagulopathy (DIVC). Septic shock is defined as sepsis with persistent hypotension despite adequate fluid resuscitation. This study focuses on patients that present with either Severe Sepsis or Septicemic Shock to the emergency department.

Many prognostic and severity parameters of sepsis have been suggested in the past such as serum lactate levels, plasma diffused arterial oxygen saturations (PaO2), percutaneous haemoglobin oxygen saturations (SpO2), central venous oxygen saturations (SvO2), severity of metabolic acidosis, C-Reactive Protein (CRP) levels, total white cell count, and hematocrit. These parameters have been well studied and documented for their role in the management of sepsis patients. These indices require high cost investments and the availability of certain specialized equipments in calculating or generating its values [2,6,7].

Being able to generate a cost effective, easily attainable parameter would greatly assist in the effective management of sepsis patients, especially in emergency departments that are sub-optimally equipped. (ie. Peripheral / sub-urban hospitals). Many Malaysian emergency departments in the peripherals / districts are not readily equipped with hematological stat laboratory equipments and arterial blood gas machines due to their high cost. The results of various blood parameters may not be immediately available upon request, potentially compromising accurate risk stratification and delaying the management of these patients.

Certain procedures such as the placement of central venous line (CVL) catheters also require time, trained personnel and additional cost which may not be easily available within the setting of smaller sub-urban hospitals. The parameters that could be gathered from insertion of a CVL and central venous blood aspiration (ie. Central venous pressure reading, severity of metabolic acidosis, central venous oxygen saturation, and hematocrit concentration) is clearly vital and plays a prognosticating role for determining survival outcome in management of patients with SIRS-sepsis spectrum [1].

Shock Index (SI)
Shock Index (SI), defined as the systolic blood pressure divided by the heart rate, is a measurement that could be readily and affordably attained. From previous studies, SI has never been studied for its value in prognosticating short-term survival to discharge for patients presenting with sepsis. This research studied the value of shock index in prognosticating short-term outcome for patients with the end spectrum of SIRS-sepsis band, namely severe sepsis and septic shock.

Majority of previous studies investigated the value of SI in the management and early detection of clinical shock for patients presenting with hemorrhage from various etiologies [9,10,11,12]. The outcome of these previous studies has proven that SI plays a role in early detection of hemorrhagic shock requiring early surgical intervention and can be reliably used as a risk-stratifying indicator for these groups of patients. As compared to visualizing the conventional vital signs (HR, SBP, DBP) on its own, SI combines these variables into a single ratio making it a comprehensive physiological variable. The critically ill patient demonstrates a physiological compensatory mechanism, keeping the blood pressure from falling despite the presence of decreased circulating blood volume, stroke volume, and cardiac output[13]. In such events, SI would serve well as an early warning indicator as compared to the conventional vital sign. The primary objective of this study is to discover if the value of SI (upon patient arrival to ED and two hours after

initial resuscitation) prognosticates the short-term outcome to discharge for patients presenting with severe sepsis and septic shock in an emergency department.

MATERIALS AND METHODS
This retrospective observational study was approved by the University of Malaya Medical Center (UMMC) Kuala Lumpur, Medical Research Ethical Review Committee. This is a pilot study conducted in the Department of Emergency and Trauma, UMMC. Patients included for this study were admitted between 1st June 2009 and 1st June 2010. Patients selected were those triaged to Resuscitation Zone 1 on arrival, and fulfilled SIRS criteria for either severe sepsis or septic shock. Patients were short-listed from the admission data registry, which noted the diagnosis containing the words "sepsis", "severe sepsis" and "septic shock". From these selected patients, only the patients who fulfilled the criteria (via retrospective review of case notes by the main investigator of the study) were included in the study. The first 50 patients fulfilled the study criteria comprised the study population.
Inclusion Criteria's:
1) Patients aged 17 and above.
2) Patients selected in the study had at least two of the four SIRS criteria's and fulfilled the requirements for either severe sepsis or septic shock.

SIRS Criteria's
- Body temperature less than 36°C or greater than 38°C
- Heart rate greater than 90 beats per minute
- Respiratory rate greater than 20 breaths per minute or, an arterial partial pressure of carbon dioxide less than 4.3 kPa (32 mmHg)
- White blood cell count less than 4000 cells/mm³ (4 x 109 cells/L) or greater than 12,000 cells/mm³ (12 x 109 cells/L), or the presence of greater than 10% immature neutrophil band forms.

Requirements for severe sepsis patients:
i) Fulfilling at least 2 or more of SIRS criteria
ii) Has an associated or suspected source of infection
iii) Has one or more of the following
- Evidence of end organ damage (eg. Elevated creatinine levels, > 120 μmol/L or altered mental status, GCS < 14)
- Serum lactate levels of equal or > 4mg/dL)
- Episode of hypotension (<90/60 mmHg), which responds to initial fluid resuscitation

Requirements for septic shock patients:
i) Fulfilling at least 2 or more of SIRS criteria
ii) Has an associated or suspected source of infection
iii) Has persistent hypotension (<90/60 mmHg) which does not respond to adequate fluid resuscitation (adequate fluids referred to as CVP 8-12 cmH20).

Exclusion Criteria's:
1) Patients aged < 17 years old
2) Patients taking medications that have significant atria-ventricular blockage effect. (Beta blockers, calcium channel blockers, digoxin and amiodarone)
3) Patients with end-stage malignancies

4) Patients with internal pacemakers
5) Patients with associated diagnosis of acute coronary syndrome
6) Patients with atrial fibrillations.
7) Patients presenting with associated upper gastrointestinal bleeding (having presenting complaints of hematemesis or diagnosed by an OGDS)
8) Patients with imuno-compromised states (on chronic steroid therapy or retroviral disease)
9) Sepsis patients with low blood pressure that were started on inotropes immediately (< 2 hours from arrival to the ED)

Patients who were started on inotropes immediately were not included in the study group due to the pottential influence of the inotrope onto the (SI 2) ratio calculated. Septic shock patients that were included were patients who failed to respond to adequate fluid resuscitation within the first 2 hours or patients that showed transient responds to fluids after which intotropic support was later initiated (>2 hours after arrival).

Triaging Method:
Triaging to Zone 1 (Resuscitation Hall) was done by a senior ED nurse who obtains a brief history and measures vital signs (heart rate (HR), blood pressure (BP), temperature (Temp), and respiratory rate (RR)) immediately on arrival. The BP was measured by an automated, upper-arm cuff inflation device in all patients. BP was measured by auscultation, when automated cuff inflation method failed to provide readings, particularly in hypo-tensive patients. Temperatures were measured orally with a standardized digital thermometer (0.5°C added to the reading for oral caliberation), and HR was measured by a continues ECG tracing on a cardiac monitor. The triage decision to allocate patients to either Zone 1 (requiring immediate treatment- seen immediately) or Zone 2 (requiring urgent treatment- seen within 30 mins) was based on patients' history of presenting illness, initial clinical evaluation, and vital signs obtained on arrival (based on a readily available objective guideline).

Data Collection:
For the purpose of the study, data was extracted from the case notes of each individual patient who fulfilled the study criteria. The information gathered was documented onto the data collection sheet. The Shock Index was calculated based on the systolic blood pressure (SBP) and the heart rate taken on arrival to the ED (SI 1), and after two hours of initial resuscitation from the time of arrival to the ED (SI 2). (The two-hour period was specified with the assumption that within this period of time adequate initial resuscitation would have already been administered for the patient). All patients that were included within the study population were seen immediately upon arrival to the ED. The HR and SBP were acquired from the vital signs chart (adopted from the patients' case notes), which was populated at least every 30 minutes in accordance to the Zone 1 (resuscitation hall) protocol. Dividing the heart rate upon the systolic blood pressure generates the shock index value. Data such as age, gender, temperature (Temp), and respiratory rate (RR), were also retrieved from the case notes.

Table I: Clinical parameter distribution of the variables stratified by death and survival to discharge.

| Predictors	Survival Median (Min, max)	Death Median (Min, max)	P-value
Demographic			
Age	62.5 (17.0, 84.0)	63.0 (24.0, 90.0)	0.648§
Gender			0.944*
Male	9 (47.4)	10 (52.6)	
Female	15 (48.4)	16 (51.6)	
Clinical			
Temperature	38.0 (35.3, 41.2)	37.5 (34.8, 39.8)	0.460§
Heart Rate	111.0 (84.0, 174.0)	120.0 (70.0, 140.0)	0.749§
Respiratory Rate	24.0 (19.0, 31.0)	25.0 (18.0, 36.0)	0.335§
(SI 1)	1.2 (0.4,1.7)	1.4 (0.8, 2.7)	0.009§
(SI 2)	0.9 (0.6, 1.1)	1.1 (0.8, 1.8)	<0.001§

§ Two-sample Wilcoxon rank sum test (Mann–Whitney U Test). *Chi-square analysis was used for statistical test, (SI 1); Shock index on arrival to Emergency Department, (SI 2); Shock index after 2 hours from arrival to the emergency department

Table II: Sensitivity, specificity analysis with respective ROC values of the significant (p <0.05) clinical parameters tested towards the outcome of survival

Parameter	Sensitivity	Specificity	ROC [95% CI]	optimal cut of
(SI 1)	54.2%	26.9%	0.2925 [0.1492, 0.4358]	≥1.2
(SI 2)	20.8%	19.2%	0.1106 [0.0264, 0.1948]	≥1.0

Table III: Sensitivity, specificity analysis with respective ROC values of the significant (p <0.05) clinical parameters tested towards the outcome of death

eter	Sensitivity	Specificity	ROC [95% CI]	optimal cut of
(SI 1)	73.1%	45.8%	0.7075 [0.5642, 0.8508]	≥1.2
(SI 2)	80.8%	79.2%	0.8894 [0.8052, 0.9736]	≥1.0
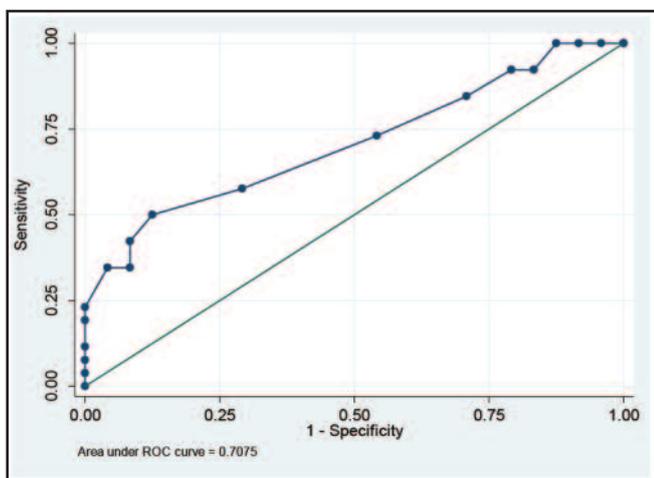
Fig. 1: ROC curve for (SI 1) versus outcome = death
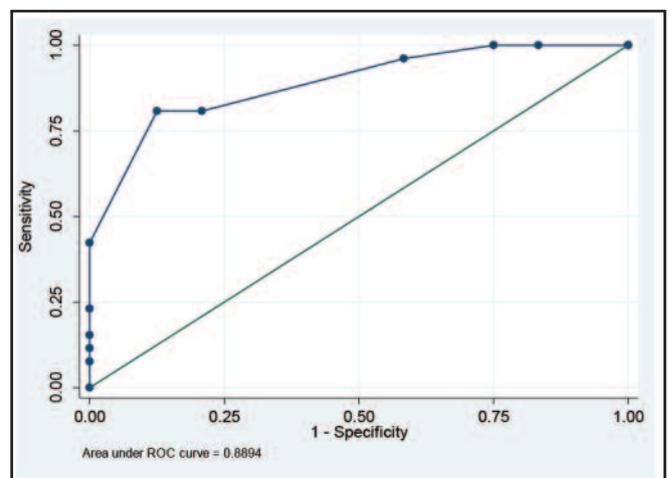
Fig. 2: ROC curve for (SI 2) versus outcome = death

Statistical Analysis:
From the values gathered, data analysis was carried out to determine the value of SI in prognosticating the short-term outcome to discharge. Analysis was also performed to determine whether other parameters that were gathered had value in prognosticating short-term outcome. Data obtained were presented in numerical variables with median, minimum and maximum values noted. The median was used due to the small sample size and the normality not assumed. The outcome is defined as either death (negative outcome) or survival (positive outcome) to discharge. Mann-Whitney U test was used to analyze the significant values amongst all the clinical parameters tested. Amongst the significant parameters attained (p value < 0.05), sensitivity and specificity analysis was carried out to attain the best cut-off point to predict outcome (death / survival to discharge). Analysis of area under the curve (AUC) with confidence interval (CI) analysis was also performed amongst these variables. This analysis was repeated for certain significant parameters in combination of each other (multiplied or divided by each other) and its sensitivity, specificity, cut-off and AUC value again determined by similar manner. Results of the analysis were then evaluated to determine whether SI and other parameters had predictive value of the short-term

outcome of patients with severe sepsis and septic shock. Data analysis was carried out using STATA 9.0 (Stata Corporation, TX, USA) software.

RESULTS

There were a total of 50 patients recruited in this pilot study. The study population comprised 19 males (38%) and 31 females (62%). The age range was between 17–84 years old (median 54.5 years). The number of severe sepsis and septic shock cases were 31 (62%), and 19 (38%) respectively. There were 17 (34%) cases of pneumonia, 13 (26%) cases of urological sepsis, 8 (16%) cases of gastro intestinal tract related infections and 12 (24%) cases of other infections. There were a total of 23 (46%) survivors and 27 (54%) deaths. The sample characteristics of the study population are presented in Table 1, stratified by death and survival to discharge. Seven clinical parameters were tested to identify the best parameter that could prognosticate the outcome namely, (SI 1), (SI 2), Age, Gender, Temp, HR, RR. Mann–Whitney U Test revealed two variables showing significant values of $p < 0.05$: The following are the significant variables namely (SI 1) (p: 0.009) and (SI 2) (p <0.001). The other five variables did not show significant values, namely HR (p: 0.749), RR (p: 0.335), age (p: 0.648), gender (p: 0.944), and Temp (p: 0.460). (SI 1) and (SI 2) were found to be reliable predictors of death. When analyzed for the outcome of death, (SI 2) shows higher sensitivity, specificity and ROC values compared to (SI 1), 80.8%, 79.2%, 0.8894 [CI95 0.8052, 0.9736] and 73.1%, 45.8%, 0.7075 [CI95 0.5642, 0.8508] respectively. The cut-off point for (SI 1) was ≥ 1.2 and (SI 2) ≥ 1.0.

ROC Curve Analysis:
ROC analyzes sensitivity, (ie. Comparing true positive rate vs. false positive rate) reflecting an objective measure of performance for a diagnostic test. There are two ROC curves tabled in this study. Figure 1, is the ROC curve drawn up for the parameter of (SI 1) tested against the outcome of death. This ROC curve demonstrates an AUC value of 0.7075 [CI95 0.5642, 0.8508]. Figure 2 is the ROC curve that challenged (SI 2) against the outcome of death. The AUC value for this parameter was 0.8894 [CI95 0.8052, 0.9736]. According to the ROC curve analysis, the best early predictor of death was (SI 2). The sensitivity, specificity and cut-off point analysis with their respective ROC values are shown in Table 2. ROC analysis graph is shown in figures 1-2.

DISCUSSION

After careful analyses of the data, (SI 2) shows high sensitivity and specificity in prognosticating death. Statistical analysis showed that gender, race, age and temperature had no significance in predicting the short-term outcome of septic shock and severe sepsis patients. The results demonstrate that (SI 1) has a high sensitivity (73.1%) but poor specificity (45.8%) in predicting mortality amongst severe sepsis and septic shock patients in the ED. The cut-off point determined for (SI 1) was ≥ 1.2. The predictive value of SI improves when it's taken after 2 hours from arrival to ED (after initial resuscitation has taken place), (SI 2). The predictive accuracy

of (SI 2) for death at a cut-off point of ≥ 1.0 has a sensitivity of 80.8% and a specificity of 79.2%. This proves (SI 2) as a sensitive and specific early predictor for death amongst septic shock and severe sepsis patients, much superior than (SI 1). Previous research that studied the utility of SI in predicting mortality amongst community acquired pneumonia patients did not include serial SI data but only a single admission SI reading[14]. Similarly a previous study involving mortality in trauma patients only documented a single SI reading for the study purpose[10]. This study demonstrates a vast difference in significance and predictive value of SI when taken at two different time point intervals. In this study, a two-hour interval period was given (after the first SI reading) from arrival to ED. The 2 hours was determined to allow adequate initial resuscitation to take place, and a physiological response to the resuscitation be evaluated on a second reading, (SI 2). Initial resuscitation would involve the stabilization of the airway, breathing and circulation components. It includes the administration of oxygen, measures of airway maintenance, intravenous fluids administration, antibiotics, antipyretics, necessary initial symptomatic treatment and procedures (eg. central venous catheter placement, placement of continues bladder drainage catheters and naso-gastric tube insertion).

The (SI 1) value is less accurate compared to (SI 2) possibly due to the fact that (SI 1) is taken immediately on arrival to the ED, giving rise to alteration of physiological parameters (ie. heart rate) due to anxiety, fear, fever or pain. The two hour phase allows time for medical staff to administer initial treatment, making the (SI 2) parameter a realistic reflection of the patients current clinical status, making it a reliable predictive index as compared to (SI 1).

Advantages of (SI 2) as a prognostic parameter:
Amongst the advantages of SI is its low cost in attaining the value, and its immediate availability as compared to other hematological or serological parameters. It is also a non-invasive parameter and does not require blood aspirations, which decreases the risk of biohazard exposure to medical staff. This is especially emphasized if the marker is required to be taken serially. The calculation of the index is simple and can be taught easily to medical support staff. This parameter would proof useful in the setting of peripheral hospitals for early detection of the critically ill patient. Attaining this marker would further assist clinicians in decision making for tertiary referrals. In hospitals, which are sub-equipped with stat laboratory equipments, this marker would proof useful as a tool in early detection of critically ill sepsis patients. The information gained from the (SI 2) would also contribute to improving effective communication amongst Emergency Physicians and relatives of patients when deciding further definitive care management.

Limitations of the study and pitfalls of SI:
Previous studies have proven SI as a sensitive index in identifying severely ill patients[15]. Nevertheless there was no evidence to suggest SI as a reliable tool that could be used to monitor the progress or outcome of resuscitation for sepsis patients. In this study, SI was proven to be valuable in prognosticating the outcome of death but was never studied for its value as a physiological parameter in determining

progress of resuscitation. Therefore SI is an index that needs to be analyzed together with other sepsis parameters in determining the course and management efficacy of the patient.

The readings of the HR and SBP can occasionally be inaccurate especially so during movement and manipulation of the patient, even more so if the measurement is done by an automated inflation cuff device which has integrated electronic recording of results. This could potentially cause the artifact error recordings to be recorded onto vital sign charting and assumed as real readings. Therefore an accurate method would be to calculate the SI based upon an average stable and reliable reading of vital signs, and not upon a single measurement. This would also constitute good clinical practice. The measure would help in avoiding artifact related errors. There have been several initiatives to create software and monitors that detect artifact related errors in vital sign readings for anesthetic and operation room purposes[16.] In this study, the SI was calculated based upon the documentation in the vital signs chart. The vital signs were documented by the nurses in charge of the patient based on real time readings during the time of charting. There is no protocol in place for charting down of average stable vitals. It is nevertheless general practice that if a vital sign is obviously erroneous then the nurse in charge would repeat the readings again for confirmation. There is no data to date that studies motion artifact related errors in measurement of vital signs in emergency departments.

This study has been conducted based on the data retrieved from patients' case notes. The reliability of the data remains subjective to the process of documentation by the staff nurses involved. This study is done with a group of 50 patients, involving only one center. The factor of treatment variability amongst various centers could possibly reflect in the treatment outcome and may affect the reliability of the results obtained. This current study would reflect well upon the population and treatment protocol involving patients within this study center (UMMC).

Suggestions for future research:
This study is a pilot study conducted with a retrospective observational design. Despite its significance, the study only involves a total number of 50 patients. Future studies should be carried out prospectively to further confirm the findings in this research. Future analysis should incorporate more details such as, measures taken during initial resuscitation, amount of fluid administered within the initial resuscitation phase, serial SI readings (> 2 readings), incorporation and comparison to other sepsis parameters such as lactate levels, SvO2, severity of metabolic acidosis, and CRP. The correlation of SI with CVP should also be studied simultaneously within the research.

CONCLUSION
(SI 2) may potentially be utilized as a reliable predictor for death in patients presenting with septic shock and severe sepsis in an emergency department. This parameters should be further analyzed in a larger scale prospective study to determine its validity.

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Background: Severe sepsis and septic shock are major causes of morbidity and mortality worldwide and need immediate medical attention. Early Results: A total of 85 patients were diagnosed as severe sepsis and septic shock with 45 female patients and mean. age 47.69 years ranging from 18 to 83 years. Pneumonia (45.9%) was found to be the major source of infection. the emergency department with a diagnosis of severe. sepsis and septic shock were included. In the United States, severe sepsis is recorded in 2% of patients admitted to the hospital. Of these patients, half are treated in the intensive care unit (ICU), representing 10% of all ICU admissions.6,7 The number of cases in the United States exceeds 750,000 per year7 and was recently reported to be rising.8 However, several factors â€" new International Classification of Diseases, 9th Revision (ICD-9) coding rules, confusion over the distinction. Outcome Before the introduction of modern intensive care with the ability to provide vital-organ support, severe sepsis and septic shock were typically le-thal. Even with intensive care, rates of in-hospital. Critical (respiratory failure, shock, or multiorgan system dysfunction): 5%. In this study, all deaths occurred among patients with critical illness, and the overall case fatality ratio (CFR) was 2.3%.(35) The CFR among patients with critical disease was 49%.(35) Among children in China, illness severity was lower than in adults, with 94% of affected children having asymptomatic, mild, or moderate disease; 5% having severe disease; and less than 1% having. CFR in the large cohort in China was elevated for patients with comorbidities, with 10.5% of those with underlying cardiovascular disease