



THE EVALUATION OF PERFUSION INDEX AS A PREDICTOR OF VASOPRESSOR REQUIREMENT IN PATIENTS WITH SEVERE SEPSIS AND SEPTIC SHOCK

An Essay Submitted for the Partial Fulfillment of the Master Degree in
Anesthesiology

By

Islam Rasmy Abdel-Fattah

Supervised by

Ass. Prof. Dr. Nashwa Nabil, MD

Assistant Professor of Anesthesiology,
Faculty of Medicine, Cairo University.

Ass. Prof. Dr. Ahmed Mohamed Mukhtar, MD

Assistant Professor of Anesthesiology,
Faculty of Medicine, Cairo University.

Dr. Hossam Mohamed El-Azizi, MD

Lecturer of Anesthesiology,
Faculty of Medicine, Cairo University.

**Faculty of Medicine
Cairo University**

2015

ACKNOWLEDGMENT

*First and foremost, thanks to **Allah**, the beneficial and the merciful.*

*I would like to express my deepest gratitude and sincere thanks to **Assistant Prof. Dr. Ahmed Mohamed Mukhtar**, assistant Professor of anesthesiology, Faculty of medicine, Cairo University, who kindly helped me a lot in this thesis. It is a great honor for me to work under his supervision with his honesty and modesty.*

*I would like also to thank **Assistant Prof. Dr. Nashwa Nabil**, assistant Professor of Anesthesiology, Faculty of Medicine, Cairo University and **Dr. Hossam Mohamed El-azizi**, lecturer of Anesthesiology, Faculty of medicine, Cairo University, for their sincere guidance and remarkable thoughts throughout the whole work.*

*I would like also to thank **Assistant Prof. Dr. Sabah Abd El-raof**, assistant Professor of Anesthesiology, Faculty of Medicine, Cairo University*

Finally, thanks for the patients who participated in the present work, hoping that this thesis would be helpful in minimizing their suffer and pain.

LIST OF ABBREVIATIONS

AKI	Acute kidney injury
ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
APACHE	Acute physiological and chronic health evaluation
ARDS	Acquired respiratory distress syndrome
AUC	Area under the curve
CDC	Centers for Disease Control
CPO	Conventional pulse oximeter
GCS	Glasgow coma scale
CVP	Central venous pressure
MAP	Mean arterial pressure
INR	International normalized ratio
PaCO ₂	Arterial carbon dioxide partial pressure
PaO ₂	Partial pressure of arterial oxygen
PcvCO ₂	Central venous carbon dioxide partial pressure

PI	Perfusion index
Pv-a CO ₂	Central venous-to-arterial blood carbon dioxide partial pressure difference
ROC	Receiver operating characteristic
SaO ₂	Arterial oxygen saturation
HR	Heart rate
ICU	Intensive care unit
ScvO ₂	Central venous oxygen saturation
SET	Signal Extraction Technology
IL	Interleukin
LPS	Lipopolysaccharide
NO	Nitric oxide
SIRS	Systemic inflammatory response syndrome
SVo ₂	Saturated venous oxygen tension
TNF	Tumor necrosis factor
WBC	White blood cells

LIST OF TABLES

<i>Table No.</i>	<i>Description</i>	<i>Page No.</i>
1	Patients characteristics	37
2	Hemodynamic and metabolic variables in study groups	38
3	Central and peripheral perfusion variables	39
4	Comparison of the areas under the ROC curves for predicting the need of vasopressors	40
5	Comparison of the areas under the ROC curves for predicting ICU mortality	40

LIST OF FIGURES

<i>Figure No.</i>	<i>Description</i>	<i>Page No.</i>
1	The Response to Pathogens	11
2	Dysregulation of neutrophil recruitment to bacterial infection in nonpulmonary tissue under normal conditions and in sepsis.	16
3	Control of coagulation in normal and inflamed vasculature	19
4	Schematic representation of the main pathophysiological mechanisms of SAE	25
5	Roc curves comparing the ability of PI, lactate, P v-a Co2 gap, and ScVO2 to discriminate the need of vasopressors in septic patients	43
6	Roc curves comparing the ability of PI, lactate, P v-a Co2 gap, and ScVO2 to discriminate the ICU mortality in septic patients	44

Abstract

The Evaluation of Perfusion Index as a Predictor of Vasopressor Requirement in Patients with Severe Sepsis and Septic Shock

Introduction: The high mortality rate observed in sepsis is not only related to the quality of management but it's also related to the complex nature of the disease. Loss of autoregulation and altered regional and microvascular blood flow jeopardize both central and peripheral tissue perfusion in septic shock. The perfusion index (PI) is derived from the photoelectric plethysmographic signal of the pulse oximeter and has shown to be a reliable monitor of peripheral perfusion in critically ill patients. These findings raise an important question: Is there any tool that can predict the requirement of vasopressor therapy in patients with severe sepsis?

Methods: All consecutive patients who were clinically suspected of having severe sepsis defined by the criteria of the American College of Chest Physicians/ Society of Critical Care Medicine Consensus Conference; were included. Upon admission to intensive care unit (ICU), hemodynamic, central and peripheral perfusion variables were simultaneously recorded at baseline. Perfusion variables included; PI, blood lactate level, central venous oxygen saturation (ScVO₂), and the difference between central venous carbon dioxide (PcvCO₂) and arterial carbon dioxide (PaCO₂) pressures (Pv-a CO₂). The primary was the use of vasopressor which was defined as any administration of vasopressor medications within 24 hours after admission to ICU.

Results: A total of 36 patients fulfilling inclusion criteria were enrolled in our study, of whom 15 died and 21 survived. Twenty-one of the 36 patients required vasopressor and 15 did not. The cutoff of the PI value was ≤ 0.3 for predicting vasopressor requirement. This cut-off value had a sensitivity of 100% and specificity of 93%; area under the curve (AUC) was 0.96 (95% CI 0.8-0.99), $p < 0.0001$. PI has a cut off value of less 0.2 to predict ICU mortality. AUC was 0.94 (95% CI 0.8-0.99), $p < 0.0001$.

Conclusion: PI less than or equal to 0.3 is predictive of vasopressor requirement during early resuscitation of patients with severe sepsis and septic shock.

Key word: Set -Roc -ScvO₂- Auc -PaCO₂ -Sovo₂

CONTENTS

	<i>Page</i>
INTRODUCTION AND AIM OF WORK	1
REVIEW OF LITERATURE	
- Epidemiology	3
- Pathophysiology of sepsis and septic shock	7
- Relation between sepsis and peripheral perfusion ...	20
- Organ and system involvement in septic patients ...	22
- Perfusion Index AND SET technology.....	26
- vasopressors therapy	30
PATIENTS AND METHODS	33
RESULTS	36
DISCUSSION	45
SUMMARY	50
REFERENCES	51
ARABIC SUMMARY	62

INTRODUCTION

Introduction

Despite various campaigns and the presence of strong evidence for management, septic shock remains the leading cause of death worldwide with in-hospital and intensive care mortality rates varying between (11.9% to 47.2%) depending on the setting and severity of disease(1).

The high mortality rate observed in sepsis is not only related to quality of management but it also relates to the complex nature of the disease. Loss of autoregulation and altered regional and microvascular blood flow jeopardize both central and peripheral tissue perfusion in septic shock(2–4). Although the relationship between systemic and peripheral circulation in patients with sepsis is not fully understood, it is clear that persistent impairment of the peripheral tissue perfusion is associated with high mortality in these patients(5). Consequently, there is a great interest nowadays, to monitor the peripheral tissue perfusion in critically ill patients. The perfusion index (PI) is derived from the photoelectric plethysmographic signal of the pulse oximeter and has shown to be a reliable monitor of peripheral perfusion in critically ill patients(6). Perfusion index is the ratio of the pulsatile to the non-pulsatile portions of the plethysmographic waveform. Because the pulsatile portion decreases with vasoconstriction and increases with vasodilatation, the changes in PI reflect changes in peripheral vasomotor tone(7).

According to Surviving sepsis campaign guidelines, vasopressor therapy should be initiated within the first 6 hours of diagnosis of sepsis, to maintain tissue perfusion, if the patients remain hypotensive despite adequate fluid resuscitation (8). More recently, a retrospective study found

a strong association between early initiation of vasopressor therapy and reduced mortality in these patients(9).These findings raise an important question: Is there any tool that can predict the requirement of vasopressor therapy in patients with severe sepsis?

Aim of the study:

The aim of the present study was to examine whether PI could predict vasopressor use during early resuscitation of patients with severe sepsis or not.

REVIEW OF LITERATURE

Epidemiology

sepsis is the second leading cause of death among patients in non-coronary intensive care units (ICUs) and the 10th leading cause of death overall in the United States(US). Furthermore, sepsis substantially reduces the quality of life of those who survive, Sepsis kill 20 to 50% of severely affected patients (10).

Centers for Disease Control (CDC) estimate that there were 450,000 cases of sepsis per year in the United States, with .100, 000 deaths. The CDC warned that the incidence was increasing(11).

Derek C. Angus found that 192,980 cases of severe sepsis in US. The mean age was 63.8 years, and 49.6%were male and suggest that national incidence rate is over 751,000 cases of sepsis are diagnosed annually, 416,700 (55.5%) had underlying co-morbidity and 160,700 (21.4%) were surgical, and resulting in more than 100,000 deaths. A retrospective analysis of data from over six million hospital discharge records estimated the incidence of severe sepsis at 3 cases per 1000 population, and 2 per 100 patients admitted to the hospital. The estimated cost of treatment for patients with severe sepsis was over 22,000 \$ per patient, or more than 16 million \$ per year(11)(12).

Although, the incidence of sepsis increased by an average of 8.7% per year between the year 1979 and 2002, the in- hospital mortality rate declined from 28 to 18 percent over the same period. The incidence of sepsis varies among ethnic groups. The contribution of various infectious organisms to the burden of disease has changed over time. Although the number of cases of gram-negative sepsis remains substantial, Gram-positive bacteria are more frequently identified among patients in the US. The incidence of fungal

sepsis, though lower than that of bacterial sepsis, has increased steadily in recent years(10).

Information from 22 ICU around Paris was used to assess the epidemiology of septic shock between 1993 and 2002. Septic shock accounted for 8.2% per 100 ICU admissions, and was associated with a 60% mortality rate(13). Alexander Melamed found that rapid rise in sepsis mortality seen in previous decades has slowed, but population ageing continues to drive the growth of sepsis-associated mortality in the United States(14).

Factors that influence the outcome:

- **Abnormal host response to infection:** Anomalies in the host's inflammatory response may indicate increased susceptibility to severe disease and mortality, Failure to develop fever is associated with increased fatality rates in patients with sepsis. Leucopenia was also more frequent in non-survivors. Thus, failure to develop febrile response and the presence of leucopenia are characteristic of severe disease, and probably represent anomalies in the host's inflammatory response (15)(16).
- **Underlying disease:** The presence of underlying disease and the functional health status of the patient are important determinants of outcome in severe sepsis (16).
- **Site of infection:** The site of infection in patients with sepsis may be important determinant of outcome. Aleksandra Leligdowicz(17)found that anatomic source of infection is associated with hospital mortality in patients who have septic shock, and that variation in mortality by source of infection is independent of predisposing factors. Hospital

mortality is highest for patients who have intra-abdominal infection secondary to ischemic bowel and disseminated infections and lowest for those who have obstructive uropathy–associated urinary tract infection (17).

- **Blood culture positivity:** Aleksandra Leligdowicz found that Infection was documented by a positive culture in 69% of patients; the remainder had no positive cultures but had definitive radiologic, surgical, autopsy, or biopsy evidence of infection. Of those who had positive cultures, gram-negative organisms accounted for 50%, gram positive organisms for 37%, anaerobic organisms for 5%, and fungi (17)(15).
- **Offending organism:** The type of micro-organism may be an important variable determining the nature and severity of the septic process. Although severe infections due to gram-negative and gram-positive bacteria appear to have a similar outcome, nosocomial blood stream infections have a worse outcome than community-acquired infections. Community-acquired infections accounted for 61% of the cases of septic shock and 37% of the patients were admitted to the ICU directly from the emergency(17)(18).
- **Antimicrobial therapy :**Intra-abdominal infection and continuous renal replacement therapy were associated with increased hospital mortality in patients with septic shock who received appropriate antimicrobial therapy (19). In contrast, Recent antibiotic exposure is associated with increased hospital mortality in Gram-negative bacteremia complicated by severe sepsis or septic shock(15)(20).