



Ain Shams University  
Faculty of Medicine  
Department of Anesthesia, Intensive  
Care and pain management

# Central venous-to-arterial carbon dioxide difference as a predictor for mortality and morbidity in septic patient

*Thesis*

Submitted for partial fulfillment of  
M.D Degree in Anesthesia and intensive care

*By*

**Khaled Mohamed Ahmed Mohamed Abdou**

M.B.B.CH., M.Sc., Anesthesia – Ain Shams University

Under supervision of

**Prof. Dr. Bahaa Al-dien Ewais Hassan**

Professor of Anesthesia, intensive care and pain management  
Faculty of Medicine – Ain Shams University

**Prof. Dr. Ahmed Nagah El Shaer**

Professor of Anesthesia, intensive care and pain management  
Faculty of Medicine – Ain Shams University

**Dr. Marwa Ahmed Khairy**

Lecturer of Anesthesia, intensive care and pain management  
Faculty of Medicine – Ain Shams University

**Dr. Amr Sobhy Abd Elkway**

Lecturer of Anesthesia, intensive care and pain management  
Faculty of Medicine – Ain Shams University





## Acknowledgement

First, thanks are all to ALLAH the most merciful for supporting me all through my life.

I would like to express my deepest gratitude to **Prof. Dr. Bahha Al-dien Ewais Hassan**, Professor of Anaesthesia and Intensive Care, Faculty of Medicine, Ain Shams University. I feel highly honored by having the chance to work under his supervision. I had the privilege to benefit from his great knowledge.

I am also very grateful to **Prof. Dr. Ahmed Nagah El Shaer**. Professor of Anaesthesia and Intensive Care, Faculty of Medicine, Ain Shams University, **Dr. Marwa Ahmed Khairy** Lecturer of Anaesthesia and Intensive Care, Faculty of Medicine, Ain Shams University, and **Dr. Amr Sobhy Abd Elkway** Lecturer of Anaesthesia and Intensive Care, Faculty of Medicine, Ain Shams University for their close supervision, fruitful advices, and the great effort they have done throughout the whole work.

*Khaled Mohamed Abdou*



# CONTENTS

	Page
Introduction	1
Aim of the work	3
Review of Literature	
Sepsis	4
Venous–arterial CO <sub>2</sub> difference as a resuscitation target in shock states	34
Patient and methods	45
Results	52
Discussion	59
Conclusion	68
Summary	69
References	71
Arabic summary	83



# LIST OF ABBREVIATIONS

Abbreviation	Meaning
ARDS	acute respiratory distress syndrome
C a–mv O <sub>2</sub>	Arterial - mixed venous O <sub>2</sub> contents difference
C a-v O <sub>2</sub>	Arterio-venous oxygen content difference
C mv–a CO <sub>2</sub>	Mixed venous to arterial CO <sub>2</sub> contents difference
C°	Celsius
CO <sub>2</sub>	Carbon dioxide
CVP	Central venous pressure
DIC	Disseminated intravascular coagulopathy
DO <sub>2</sub>	Oxygen delivery
F	Fahrenheit
HPV	hypoxic pulmonary vasoconstriction
ICU	Intensive care unit
MAP	Mean arterial blood pressure
MODS	multiple organ dysfunction syndrome
O <sub>2</sub>	Oxygen
P cv- art CO <sub>2</sub> gap	Central Venous–arterial CO <sub>2</sub> difference
P mv- art CO <sub>2</sub> gap	Mixed Venous–arterial CO <sub>2</sub> difference
PaCO <sub>2</sub>	Arterial carbon dioxide tension

PaO <sub>2</sub>	Arterial oxygen tension
PcvCO <sub>2</sub>	Central venous carbon dioxide tension
PcvO <sub>2</sub>	Central venous oxygen tension
PEEP	Positive end-expiratory pressure
qSOFA	quick Sequential Organ Failure Assessment
RQ	Respiratory quotient
SaO <sub>2</sub>	Arterial oxygen saturation
SAPS II	Simplified Acute Physiology Score II score
ScvO <sub>2</sub>	Central venous oxygen saturation
SIRS	Systemic inflammatory response syndrome
SOFA	Sequential Organ Failure Assessment
VCO <sub>2</sub>	Carbon dioxide production
VO <sub>2</sub>	Oxygen consumption



# LIST OF TABLES

<b>Table NO</b>	<b>Title</b>	<b>Page No.</b>
1	Risk factors for sepsis:	5
2	Sequential [Sepsis-Related] Organ Failure Assessment Score (SOFA) score	10
3	Definition and Diagnostic criteria for sepsis Infection	45
4	Baseline values	53
5	Source of sepsis	54
6	lactate values between both groups at T6 and T12	54
7	SOFA Score between the two groups at T24 and D15	56
8	ICU length of stay	57
9	28 day mortality between two groups	57
10	P(cv-a) CO2 between survivors and non-survivors	58



## LIST OF FIGURES

<b>Table NO.</b>	<b>Title</b>	<b>Page No.</b>
1	The Host Response in Severe Sepsis	14
2	Identifying Acute organ dysfunction in sepsis	22
3	Central venous O2 saturation values	37
4	Causes of lactate excess	38
5	Cori cycle	38
6	The model for lactic acid buffering by bicarbonate, explaining the relative increase of CO <sub>2</sub> during “non-aerobic metabolism”	41
7	Vo <sub>2</sub> and VCO <sub>2</sub> response in cases of shock states	43
8	Flow chart of the patients distribution	52
9	CO <sub>2</sub> gap and lactate evolution	55
10	lactate clearance in high and low co <sub>2</sub> gap groups	55
11	CO <sub>2</sub> gap groups and SOFA score progression	56
12	Survivors and non-survivors in relation to CO <sub>2</sub> gap	58



# INTRODUCTION

Current guidelines for hemodynamic management of severe sepsis and septic shock recommend the use of global markers of tissue hypoxia as resuscitation endpoints (*Dellinger et al., 2013*).

In the initial resuscitation period, targeting either central venous oxygen saturation (ScvO<sub>2</sub>) normalization or lactate clearance, or the combination of both, is accepted (*Jones et al., 2010*).

However, each one of these two variables have its own limitations. Although the use of ScvO<sub>2</sub> seems to provide more real-time information than lactate clearance, the nature of septic conditions, characterized by microcirculatory heterogeneity that generates capillary shunting, is frequently accompanied by elevated ScvO<sub>2</sub> values. Indeed, abnormally high ScvO<sub>2</sub> values have been associated with increased mortality in septic shock patients (*Textoris et al., 2011*).

However achievement of the recommended normalized ScvO<sub>2</sub> values during the initial resuscitation therefore does not rule out persistent tissue hypoxia, and some authors consider that ScvO<sub>2</sub> should be used in combination with other tissue perfusion endpoints (*Van Beest et al., 2011*).

On the other hand, despite lactate clearance being proven to be as beneficial as ScvO<sub>2</sub> in guiding resuscitation in sepsis, at the bedside the clinician has to

## ***Introduction***

face the uncertainty of a high lactate value, without knowing whether this lactate reflects persistence of hypoperfusion or whether its normalization is just a matter of time (*Andersen et al., 2013*)

On the whole, elevated lactate values could lead to unnecessary interventions, with their potential deleterious effects, such as tissue edema and increased fluid balance, which have consistently been associated with worse outcome (*Boyd et al., 2011*).

Recently, some authors have advocated that the central venous-to-arterial carbon dioxide difference P (cv-a) CO<sub>2</sub> might be complementary tools to identify patients with persistent global hypoperfusion (*Vallet et al., 2013*).

Certainly, partial pressure of carbon dioxide gap has demonstrated its prognostic value in different conditions, and a cutoff value of 6 mmHg seems to reflect whether global flow is adequate (gap <6 mmHg) or insufficient (gap ≥6 mmHg) (*Ospina-Tascon et al., 2013*).

Tissue partial pressure of carbon dioxide (PCO<sub>2</sub>) reflects metabolic alterations due to inadequate perfusion in actively metabolized tissues. The PCO<sub>2</sub> gap, which has been shown to be inversely related to cardiac output (CO), is considered as a marker of the ability of the venous blood flow to remove the CO<sub>2</sub> excess produced in tissues. Thus, an impaired tissue perfusion during a reduced blood flow is the main determinant of a rise of the PCO<sub>2</sub> gap (*Futier et al., 2010*)

## **Aim of the work:**

The purpose of this study is to evaluate the clinical relevance of high value of the  $P(cv-a)CO_2$ , and its relationships to other markers of impaired tissue perfusion and oxygenation (blood lactate) and if it can be used as a predictor for mortality and morbidity in septic patients.