# MONITORING AND OPTIMIZATION OF TISSUE OXYGENATION IN CRITICALLY ILL PATIENTS

#### An Essay

Submitted for Partial Fulfillment of Master Degree
In Intensive Care

# By Reda Ramadan Abd Elbakey $\mathcal{M}.\mathcal{B}.,\,\mathcal{B}.\mathcal{C}\hbar$

Under Supervision of

Prof. Dr. Ahmed Mohammed Elsaid El-Henawy

Assistant Professor of Anesthesiology and Intensive Care

Faculty of Medicine, Ain Shams University

**Dr. Mohammed Abd Elsalam El-Gendy**Lecturer of Anesthesiology and Intensive Care
Faculty of Medicine, Ain Shams University

Faculty of Medicine Ain Shams University 2014



First of all, my deepest and greatest gratitude and thanks to **God** for helping and supporting me to present this modest work.

In fact, I can't find meaningful words to express my extreme thankfulness, profound gratitude and deep appreciations to my eminent Prof. Dr. Ahmed Mohammed Elsaid El-Henawy, Assistant Professor of Anesthesiology and Intensive Care, Faculty of Medicine- Ain Shams University, for his majestic generous help, guidance, kind encouragement and great fruitful advice during supervision of this work.

Also I'm deeply grateful to Dr. Mohammed Abd Elsalam El-Gendy, Lecturer of Anesthesiology and Intensive Care, Faculty of Medicine-Ain Shams University, who supported me through devoting his time, great efforts and unlimited experience to facilitate the production of this work.

Finally, I would like to express my deepest thankfulness to my **Family** for their great help and support whom without I could do nothing.



Reda Ramadan Abd Elbakey

## **Contents**

List of Abbreviations	I
List of Figures	<b>VI</b>
List of Tables	<b>VIII</b>
Introduction	1
Aim of the Work	3
Review of Literature	
- Chapter (1): Physiology of Tissue Oxygenation	4
- Chapter (2): Pathophysiology of Abnormal	Tissue
Oxygenation in Critically Ill Patient	48
- Chapter (3): Monitoring of tissue oxygenation	99
• Upstream	103
• Downstream	136
- Chapter (4): Optimization of tissue oxygenation	162
Summary	212
References	217
Arabic Summary	<b></b>

# List of Abbreviations

Abb.	Mean
AABB	American Association of Blood Banks
ACS	Abdominal Compartment Syndrome
ACS	American College of Surgeons
ADH	Anti-diuretic hormone
ADP	Adenosine diphosphate
AKI	Acute kidney injury
ALBIOS	Albumin Italian Outcome Sepsis Study
ALI	Acute lung injury
AMP	Adenosine monophosphate
ANP	Atrial natriuretic peptide
ARDS	Acute Respiratory Distress Syndrome
ATP	Adenosine Triphosphate
AVP	Arginine Vasopressin
BGB	Blood Gas Barrier
BNP	Brain natriuretic peptide
BP	Blood pressure
BSA	Body Surface Area
BTS	British Thoracic Society
cAMP	cyclic adenosine monophosphate
CaO2	arterial blood 02 content
cGMP	Cyclic guanosine monophosphate
CI	Cardiac index
CO	Cardiac Output
CO2	Carbon dioxide
COHb	Carboxyhemoglobin
COPD	Chronic obstructive pulmonary disease
CRT	Capillary Refill Time
CVC	Central venous catheter
CVP	Central Venous Pressure
DBP	Diastolic Blood Pressure
DO2	Oxygen Delivery
DO2crit	Critical DO2

Abb.	Mean
dPCO2	The arterio-venous carbon dioxide tension
	difference
DPG	Diphosphoglycerate
dVR	Pressure gradient of venous return
ECOM	Endotracheal cardiac output monitor
EDM	Esophageal Doppler monitor
EF	Ejection fraction
EGDT	Early goal directed therapy
eNOS	Endothelial NO synthase
EPSS	point septal separation
EtCO2	The end-tidal pressure of expired CO2
EVLW	Extravascular lung water
F	Fraction of the gas
FAD	Flavin adenine dinucleotide
FiO2	Fraction of Inspired Oxygen
FTc	Flow time corrected for heart rate
g/dL	Grams per deciliter
GDT	Goal directed therapy
GEDI	Global end-diastolic index
GEDV	Global end diastolic volume
HALI	Hyperoxic acute lung injury
Hb	Hemoglobin
HcueArt	Arterial blood Hb measurement by CO-
	Oximetry
HcueCap	Capillary blood Hb measurement by CO-
	Oximetry
HFOV	High frequency oscillatory ventilation
HIF	Hypoxia-inducible transcription factor
HR	Heart Rate
ICU	Intensive care unit
ITBV	Intrathoracic blood volume
IVC	Inferior vena cava
kPa	kilopascals
LiDCO	Lithium dilution cardiac output monitor
LVEDA	LV end-diastolic area

Abb.	Mean
LVEDA	LV end-diastolic area
LVSWI	left ventricular stroke work index
MAP	Mean arterial blood pressure
MetHb	Methemoglobin
MI	Myocardial infarction
MODS	Multi-organ Dysfunction Syndrome
mPAP	Mean pulmonary artery pressure
NAD	Nicotinamide Adenine Dinucleotide
NE	Norepinephrine
NIRS	Near-infrared spectroscopy
NO	Nitric oxide
NPPV	Noninvasive positive pressure ventilation
02	oxygen
O2 ER	oxygen extraction ratio
OPS	Orthogonal polarization spectral
P	Partial Pressure
P (A-a) 02	Alveolar-arterial oxygen gradient
P50	PO2 at which hemoglobin is half saturated
PAC	Pulmonary Artery Catheter
PACO2	Alveolar CO2 Partial pressure
PaCO2	Partial pressure of CO2 in arterial blood
PAO2	Alveolar Oxygen Tension
Pa02	Partial pressure of oxygen in arterial blood
Pa02	Arterial oxygen partial pressure
PAOP	Pulmonary artery occlusion pressure
PAP	Pulmonary artery pressure
PATM	Total Atmosphere Pressure
PbtO2	Intracellular PO2 values in brain tissue
PCAO	Precise control of arterial oxygenation
PCO2	Partial Pressure of CO2
PCR	Polymerase chain reaction
PCWP	Pulmonary capillary wedge pressure
PEEP	Positive End Expiratory Pressure
PgCO2	gastric intra-mucosal carbon dioxide pressure
PH2O	Partial Pressure of water

Abb.	Mean
Pi	Inorganic phosphate
PI	Perfusion index
PiCCO	Pulse Index Contour Cardiac Output
PLR	Passive leg raise
Pmsf	Mean systemic filling pressure
PO2	partial pressure of oxygen
POC	Point-of-care
PPG	Photo-plethysmograph
PPV	Pulse pressure variation
PRAM	Pressure recording analytic method
PslCO2	Sublingual partial pressure of CO2
PvCo2	Partial pressure of CO2 in mixed venous blood
Pv02	Partial pressure of oxygen in mixed venous
	blood
PVRI	Pulmonary vascular resistance index
RAP	Right atrial pressure
RBC	Red Blood Cell
RBCT	Red blood cell transfusions
ROS	Reactive Oxygen Species
RR	Respiratory Exchange Ratio
RUSH	Rapid Ultrasound in Shock
RVR	Resistance to venous return
RVSWI	right ventricular stroke work index
SAFE	Saline vs Albumin Fluid Evaluation
Sa02	Arterial haemoglobin oxygen saturation
SBP	Systolic blood pressure
Scv02	Central venous oxygen saturation
SDF	Sidestream dark-field
SI	system The International System of Units
SIRS	Systemic inflammatory response syndrome
SO2	Hemoglobin Saturation
SpHb	Hb measurement with Pulse CO-Oximetry
SpO2	Pulse oximetry SO2
SPV	systolic pressure variation
StO2	Tissue hemoglobin oxygen saturation

Abb.	Mean
SV	stroke volume
SVI	Stroke volume index
SvO2	Mixed venous oxygen saturation
SVR	Systemic Vascular Resistance
SVRI	Systemic Vascular Resistance Index
SVT	Supra-ventricular tachycardia
SVV	Stroke volume variation
TACO	Transfusion-associated circulatory overload
tCO2	Tissue CO2
TEE	Transesophgeal echocardiography
TNF	Tumor necrosis factor
tPO2	tissue oxygen tension
TPR	Total peripheral resistance
TRACS	Transfusion Requirements after Cardiac
	Surgery
TRALI	Transfusion-related acute lung injury
TRICC	Transfusion Requirements In Critical Care
TRIM	Transfusion-related immunomodulation
UOP	Urine output
V' A/Q'	Ventilation-Perfusion ratio
V'A	Alveolar ventilation
V'CO2	Volume of CO2 in Expired gas per minute
VILI	Ventilator-associated lung injury
VIP	Vasoactive intestinal polypeptide
VO2	Oxygen consumption
VR	Venous Return
Vs	stressed volume

## List of Figures

Figure	Title	Page
1	The oxygen transport system	5
2	PO2 from the atmosphere to mitochondria	8
3	gas exchange portion of the lung	10
4	Physiologic dead space	11
5	Effect of ventilation on PAO2, SO2 and PACO2	13
6	Blood movement through the alveolar-capillary membrane	15
7	Oxygen-hemoglobin dissociation curve	18
8	Circulatory system and Blood Flow	21
9	Microcirculation	23
10	Krogh's model of tissue oxygenation	24
11	Cardiac output regulation	28
12	Factors regulating blood flow	33
13	Generation of O2 Sink	42
14	The ATP cycle	44
15	Sources of ATP production	47
16	Critical oxygen delivery (DO2)	59
17	Types of shock	63
18	Alterations in global and peripheral blood flow during shock	67
19	Relative frequencies of the main types of shock	70
20	Signs of Tissue Hypoperfusion	71
21	Changes in mean aortic pressure as CO falls	76
22	Definition of sepsis	81

Figure	Title	Page
23	Microcirculation in Sepsis	85
24	Hypoxic Injury	95
25	Hyperoxaemia reduce tissue blood flow	98
26	Flow Diagram of the Components of DO2	100
27	Markers of resuscitation adequacy	102
28	Absorption spectra of normal adult haemoglobin	106
29	Frank-Starling curves	122
30	Doppler tracings of aortic blood flow recorded	133
31	Venous oxygen saturation in different venous systems	139
32	O2 Consumption-Delivery Balance	163
33	A suggested approach to transfusion in critical care	183
34	Step-wise haemodynamic approach	187
35	Fluid management algorithm	189
36	The ScvO2-dCO2-guided protocol	191
37	Macrocirculatory versus tissue perfusion resuscitation endpoints	193
38	relationship between volume status and complications	195
39	Schematic representation of the cardiac function curve	197

#### List of Tables

Table	Title	Page
1	Regional Differences in Blood Flow, Oxygen Use	27
2	Types of Hypoxemia Based on duration development	50
3	Causes of hypoxemia	51
4	Causes of a raised PaCO <sub>2</sub> (hypercapnia)	54
5	Signs symptoms with hemorrhage	73
6	The adverse effects of hyperoxia	96
7	Causes of hypoxemia	105
8	PAC Derived cardiovascular and oxygen parameters	119
9	Indications for Pulmonary Artery Catheter	120
10	Advantages and disadvantages of CO monitoring Methods	130
11	Signs and Symptoms of Organ Hypoperfusion	138
12	Changes leading to alteration in venous saturation	139
13	BTS guidelines on critical illness requiring high flow $O_2$	167
14	Combinations of Oxygen and PEEP	172

Table	Title	Page
15	Potential rules for implementing permissive hypoxaemia	176
16	Pharmacologic Effects of Vasopressors and Inotropes	203
17	Relative Effects of Changes in PaO2, Hb, and Q'T on DO <sub>2</sub>	210

#### Introduction

Despite improvements in resuscitation and supportive care, progressive organ dysfunction occurs in a large proportion of patients with acute, life threatening illness. It has been proposed that the multi-organ dysfunction syndrome (MODS) of the critically ill is a consequence of tissue dysoxia attributable to inadequate oxygen delivery, often exacerbated by a microcirculatory injury and increased tissue metabolic demands (distributive hypoxia) (*Ince & Sinaasappel*, 1999).

This may be further compounded by cytopathic hypoxia attributable to mitochondrial dysfunction (*Fink*, 2002).

So, Maintenance of tissue perfusion is critical, because global tissue hypoxia is a key step toward multiple organ failure (*Rivers et al.*, 2001).

Emerging data suggest that early aggressive resuscitation of critically ill patients may limit and/or reverse tissue dysoxia and progression to organ failure and improve outcome. Hemodynamic monitoring is essential to resuscitation efforts based on attaining specified targets (*Dellinger et al.*, 2008).

When resuscitation goals for CVP and MAP have been achieved, additional measurements of venous oxygenation and lactate may reveal inadequate tissue oxygenation indicating that additional resuscitation efforts are required (*Rady et al.*, 1996).

Both invasive and noninvasive monitoring tools have been used in critically ill patients in an attempt to optimize resuscitation. Most of these technologies focus on "upstream" markers of resuscitation and provide information on cardiac output and fluid responsiveness (Marik & Baram, 2007).

In this respect, the pulmonary artery catheter (PAC) was regarded as the gold standard, as it provides an accurate estimate of the cardiac output and can be used to determine fluid Responsiveness (*Ganz et al.*, 1971).

However, the role of invasive hemodynamic monitoring in critically ill patients is controversial as the PAC has not been proven to improve patient outcome. Furthermore, the PAC does not provide enough information about the adequacy of tissue oxygenation, i.e., "downstream" markers (*Marik & Baram*, 2007).

Alternatively, it has been argued that measurements of oxygenation at the level of specific tissues offer more sensitive information (*Ward et al.*, 2001).

Therefore, measurements of tissue perfusion and oxygenation are necessary to determine whether the ultimate goal of resuscitation, and adequate oxygen supply to tissues, has been attained (*Ahrens*, 2006).

#### **Aim of the Work**

The aim of this study is to highlight currently available devices for hemodynamic monitoring as well as techniques for assessing the adequacy of organ perfusion, tissue oxygenation and available modalities that can be used to improve tissue oxygenation.