MEASUREMENT OF AORTIC FLOW IN RESPONSE TO FLUID USING ESOPHAGEAL DOPPLER AND MONOCYTE CD 86 EXPRESSION AS PROGNOSTIC MARKERS OF POST-INFLAMMATORY IMMUNODEFICIENCY IN CRITICALLY ILL PATIENTS

Thesis

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بسم الله الرحمن الرحيم
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(١١٣)

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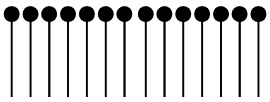
LIST OF ABBREVIATIONS

Abbrev.	Meaning
ABF	Arterial blood flow.
ACTH	Adreno-Corticotropin hormone.
ADC	Analog to digital converter.
ALI	Acute lung injury.
APACHE	Acute physiology and chronic health education.
ARDS	Acute respiratory Distress syndrome.
CO	Cardiac output.
CRH	Corticotropin-releasing hormone.
CRP	C-reactive protein.
CVP.	Central venous pressure
DO_2	Oxygen delivery.
EDM	Esophageal Doppler monitoring.
FTC	Flow time corrected for heart rate.
ICU	Intensive care unit
IL-1	Interleukin-1
LPs	Lipo-poly-saccharine.
MAP	Mean arterial pressure.
MDF	Myocardial depressant factor
MHC-II	Major Histo-compatibility complex Class II.
MODS	Multi-organ dysfunction syndrome.
No	Nitric oxide.
PACs	Pulmonary artey Catheters.
PCT	Procalcitonin
PEEP	Positive end-expiratory pressure.
PMT	Photomultiplier tube.
rAPC	Recombinant activated protein C.
$SCVO_2$	Central venous oxyhemoglobin saturation
SIRS	Systemic inflammatory response syndrome.
SNP	Single nucleotide polymorphism.
SOFA Score	Sequential organ failure assessment score.
SV	Stroke volume.
TCR	T-cell receptor
TNF	Tumor necrosis factor.
VO_2	Oxygen consumption.



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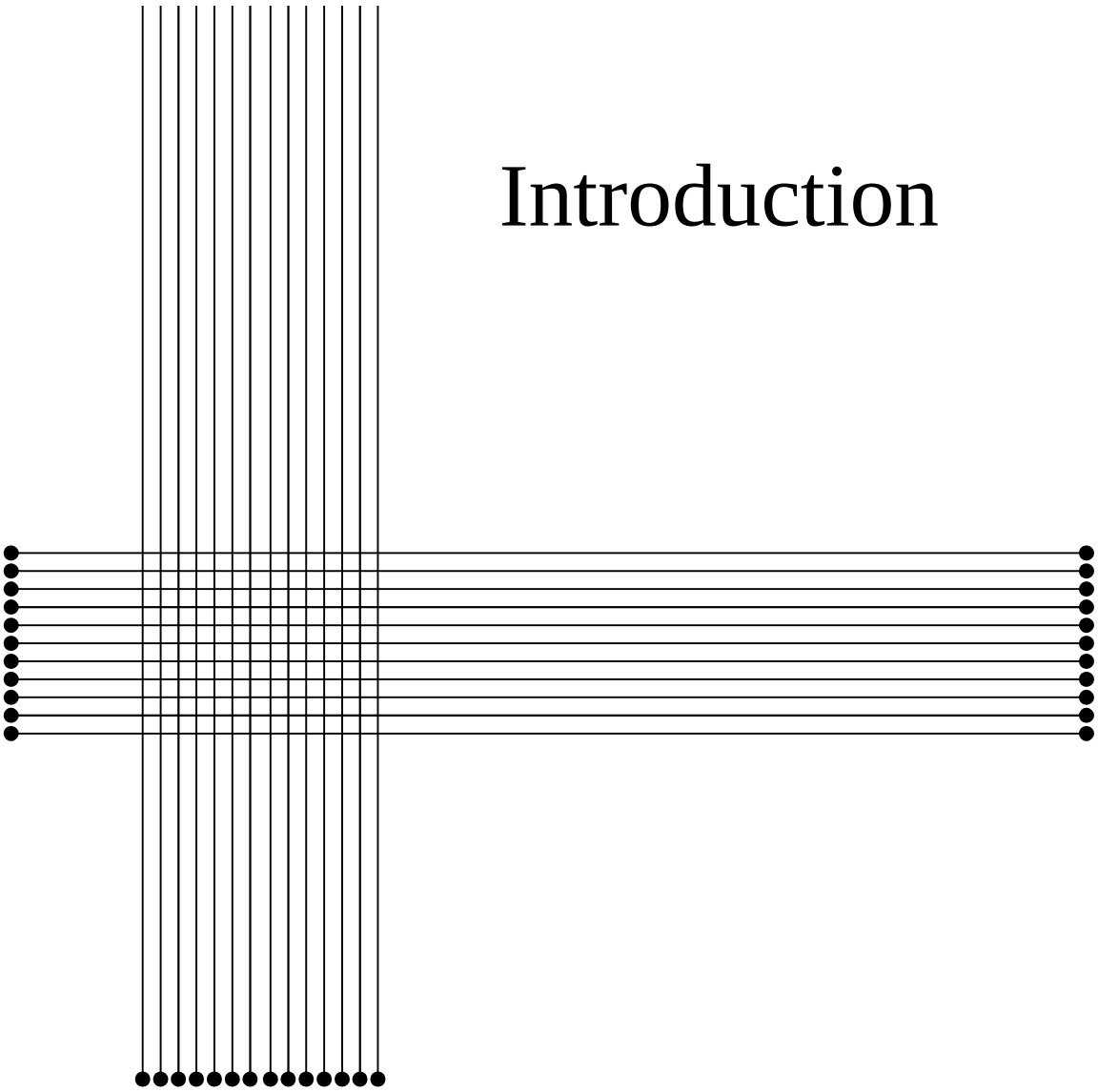

Introduction

INTRODUCTION

Major surgery, poly trauma, burns, stroke and pancreatitis are often accompanied by a massive activation of the immune system called systemic inflammatory response syndrome ***(Hotchkiss et al., 2003).***

Due to counter regulatory mechanisms such as endocrine, paracrine or autocrine actions along with intracellular alterations this hyper-inflammation is followed by a temporary immunodeficiency called compensatory anti-inflammatory response syndrome. In its most severe form it is also referred to as immune paralysis state ***(Kerstin et al., 2007).***

Post-inflammatory immunodeficiency frequently becomes life threatening since patients are predisposed to contract nosocomial infection. However, these infections are difficult to identify since they are scarcely associated with any clinical signs. Moreover, these infections can not be fought by the enfeebled immune system of such patients and may evolve into sepsis. It is therefore not surprising that sepsis and resultant multiple organs failure are the most common causes of death in intensive care units ***(ICUs) (Kerstin et al., 2007).*** In fact, in the United States alone more than 200,000 patients die of sepsis each year ***(Angus et al., 2001).***

The mechanisms responsible for post-inflammatory immuno-deficiency are not clear, which is the reason why no causal therapy has been established to date ***(Docke et al., 1997).*** Most probably, monocytic cells play a key role in the development and maintenance of this state. This monocytic cells seem to be impaired in their antigen presentation and inflammatory capacity. In fact, blood monocytes show a strongly

reduced expression of major histocompatibility complex class II (MHC-II) and produce only minor amounts of pre-inflammatory cytokines in response to bacterial lipo-polysacchafrides (LPs) ***(Docke et al., 1997).*** The magnitude of MHC-II reduction correlates with increased susceptibility to infection and subsequent mortality and is used for diagnosis of post-inflammatory immunodeficiency ***(Kerstin et al., 2007).***

MHC-II molecules are essential for the activation of $CD4^+$ cells and therefore for the initiation of any adaptive immune response and enhancement of the innate immunity ***(Hershman et al., 1990).***

In fact, the engagement of the T-cell receptor (TCR) with MHC-II complexed with antigenic peptides delivers a stimulatory signal to $CD4^+$ cells ***(Volk et al., 1991)***.

However, naïve $CD4^+$ cells in particular need to receive a second signal set from Co-stimulatory molecules for activation. One of the most important Co-stimulatory molecule is blood antigen presenting cells from ICU patients is CD86 ***(Kerstin et al., 2007).***

Esophageal Doppler monitoring (EDM) is a minimally invasive method for continuous measuring of blood flow in the descending thoracic aorta ***(Dark et al., 2004).***

Since a relatively fixed proportion of total flow travels down the thoracic aorta, descending aortic blood flow (ABF) is considered a reliable estimate of cardiac output and its change ***(Dark et al., 2004).***

Esophogeal Doppler monitoring allows monitoring of the hemodynamic effects of ionotropic drugs ***(Carious et al., 1998)*** and volume replacement ***(Roeck et al., 2003).***

Furthermore, it was recently demonstrated that Esophageal Doppler monitoring enables one to predict fluid responsiveness, either by assessing the hemodynamic effects of passive leg raising ***(Monnet et al., 2006)*** or by measuring the respiratory variation of aortic blood flow ***(Monnet et al., 2005)***.

Thus hypotensive patients with acute circulatory failure, restoration of an adequate mean arterial pressure may be associated with changes in aortic diameter that could significantly influence the circulation of aortic blood flow. If aortic diameter and flow increase with fluid loading with increasing arterial pressure then the estimated increase in aortic blood flow assuming a constant aortic diameter would be less than the true increase in aortic blood flow ***(Signer et al., 1989).***