شبكة المعلومات الجامعية

# بسم الله الرحمن الرحيم



# شبكة المعلومات الجامعية

# التوثيق الالكتروني والميكروفيلم


شبكة المعلومات الجامعية

# جامعة عين شمس

## التوثيق الإلكتروني والميكروفيلم

# قسم

## نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها علي هذه الأقراص المدمجة قد أعدت دون أية تغيرات


# يجب أن

## تحفظ هذه الأقراص المدمجة بعيدا عن الغبار

# The comparison of procalcitonin guidance in administration of antibiotic with empirical antibiotic therapy in critically ill patients with SIRS admitted in intensive care unit

**Thesis**

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in General, Intensive Care

**By**


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| | |
|---|---|
| **ABGs** | Arterial blood gases |
| **ALI** | Acute lung injury |
| **ALT** | Alanine aminotransferase |
| **ARDS** | Acute respiratory distress syndrome |
| **AST** | Aspartate aminotransferase |
| **AUROC** | Area under the receiver operating characteristics |
| **CALC-1** | Calcitonin I |
| **CCP-I** | Carboxyterminus peptide I |
| **CDC** | Centers for Disease Control and Prevention |
| **CGRP** | Calcitonin gene-related peptide |
| **CO** | Cardiac output |
| **COPD** | Chronic obstructive pulmonary disease |
| **CRP** | C-reactive protein |
| **CT** | Calcitonin |
| **DAMPs** | Damage-associated molecular patterns |
| **DIC** | Disseminated intravascular coagulation |
| **DO2** | Oxygen delivery |
| **DVT** | Deep vein thrombosis |
| **ED** | Emergency department |
| **EIP** | Emerging infections program |
| **FDA** | Food and Drug Administration |
| **GI** | Gastrointestinal |
| **IL** | Interleukin |
| **ISTH** | International society of thrombosis and hemostasis |
| **LPS** | Lipopolysaccharide |
| **MODS** | Multiple organ dysfunction syndrome |
| **PAF** | Paroxysmal atrial fibrillation |
| **PAMPs** | Pathogen-associated molecular patterns |
| **PCT** | Procalcitonin |
| **PEEP** | Positive end expiratory pressure |
| **PT** | Prothrombin time |
| **SIC** | Sepsis induced coagulopathy |
| **SIRS** | Systemic inflammatory response syndrome |
| **TNF** | Tumor necrosis factor |
| **WBC** | White blood cell |

# Introduction

The critically ill patients with sepsis usually undergo antibiotic empirical treatment. This strategy results in antibiotic overuse and increase in the cost and bacterial resistance. These patients initially present with systemic inflammatory response syndrome (SIRS). SIRS is seen after trauma, major operation, severe inflammation and infections **(Bone RC et al, 2009)**

Patients with SIRS undergo supportive therapy except SIRS due to an infection that is diagnosed as sepsis and needs early administration of antibiotic and control of infection. The prognosis of sepsis is worse than SIRS and differentiation between them is vital for the intensivist. Outcomes of critically ill patients with sepsis can improve if these patients receive prompt and appropriate antibiotic therapy **(Dellinger RP et al, 2008).**

The diagnosis of sepsis in critically ill patients is probably delayed because sign and symptoms of infection can be missing due to alteration in immune status as well as the exposure to specific treatment and procedures. In addition, because of the low specificity of diagnosis of sepsis in critically ill patients and fear of not treating life-threatening infection, leads intensivist to overuse of antibiotics in ICU **(Herbert et al., 2013).**

These issues lead to the development of new biomarkers that accurately predict sepsis in these patients. Previous studies have showed that serum level of procalcitonin (PCT) increased in patients with sepsis, and this marker is accurate in the diagnosis of sepsis. Normal serum levels of PCT are below 0.5 ng/mL and patients with serum levels above 2 ng/mL are more likely to develop sepsis **(Reinhart K et al, 2006).**

It was shown that PCT is a useful guide for initiation of antibiotic in patients with respiratory infection. Moreover, PCT-guided treatment can decrease the duration of antibiotic therapy in critically ill patients. Also, one study concluded that PCT guide treatment in patients with lower tract respiratory infection decreased antibiotic consumption up to 46.4% and clinical outcomes, and mortality were similar to patients who underwent empirical antibiotic treatment **(Müller B et al, 2010).**

# Aim of Work

The aim of this study is to evaluate the effectiveness of serum procalcitonin level as a guide for antibiotic prescription in critically ill patients with SIRS without evidence of infection in intensive care unit.

# Chapter (I)

# Systemic Inflammatory Response Syndrome

## Definition of SIRS

The distinction between SIRS and sepsis centers upon the presence or absence of a focus of infection. Thus, the identification of SIRS does not confirm a diagnosis of infection or sepsis since the features of SIRS can be seen in many other non-infective conditions. Non-infective causes of SIRS include acute pancreatitis, burns, trauma, or following major elective surgery (Fig. 1). On the other hand, sepsis is defined as a SIRS in which there is an identifiable focus of infection caused by bacterial pathogens, viruses, fungi, and parasites. Of the patients with SIRS associated with infection, the majority have Gram-negative sepsis **(Willatts et al., 2012).** Although differing etiologies present an identical clinical picture, the failure to identify causal pathogenic microorganisms does not necessarily mean that bacterial pathogens are absent, owing to the limitation of current diagnostic techniques **(Marshall and Sweeney, 2011).**

At least two criteria are required for the identification of SIRS. Thus, SIRS are manifested by two or more of the following conditions: temperature >38°C or <36°C; heart rate >90 beats/ min; respiratory rate >20 breaths/min or PaCO2 <32 torr (<4.3 kPa); WBC >12,000 cells /mm3, <4000 cells /mm3 or >10% immature (band) forms **(Bone et al., 2010).** The ACCP/SCCM has also recognized progression in the disease state from simple SIRS / sepsis to severe SIRS/sepsis in the presence of acute organ dysfunction, hypotension, or hypo perfusion. However, it should be noted that the SIRS criteria cannot perform much better for diagnosis or as a measure of prognosis, perhaps because they are too wide **(Bone et al., 2010)**.

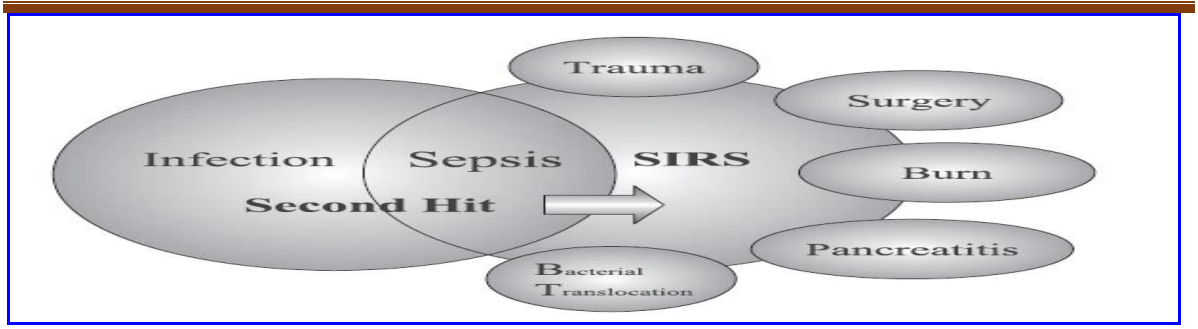


**Fig. 1.** The concept of SIRS as a common response to many initiating circumstances. The interrelationship between SIRS, sepsis, and infection is shown. **(Bone et al., 2010).**

Patients with an attack of SIRS who survive the initial inflammatory insult may die following a relatively minor second event that would not normally be life threatening **(Moore and Moore, 2015).** According to the two-hit hypothesis, the initial overactive SIRS such as acute pancreatitis somehow primes the inflammatory response. Recovery is possible if no further insult occurs. Bacterial infection as a relatively minor secondary attack will, however, lead to an exaggerated secondary inflammatory response and possibly death. Thus, the septic complications of acute pancreatitis can manifest themselves as an exaggerated SIRS response with consequent multiple organ failure and death **(Bhatia et al., 2010).**

## Clinical features of SIRS

The defining clinical features of SIRS are disturbance of body temperature, tachycardia, hyperventilation and alteration in white blood cell count. The image of a patient who is non-specifically described as ‘septic’ or ‘toxic’ with sweating, fever, chills and hypotension will be familiar to most clinicians. A frequent complication of SIRS is MODS. Dysfunction is defined as an inability of the organ to maintain homeostasis. Any organ system can become dysfunctional as a result of SIRS, and the number of organ systems involved is directly related to mortality **(Bone et al., 2012).** The most important manifestations of MODS in SIRS include the spectrum of acute lung

injury (ALI) and acute respiratory distress syndrome (ARDS) and cardiovascular derangement **(Herbert et al., 2013).**

## Etiology

The etiology of systemic inflammatory response syndrome (SIRS) is broad and includes infectious and noninfectious conditions, surgical procedures, trauma, medications, and therapies. The inciting molecular stimuli inducing the above generalized inflammatory reaction fall into two broad categories, pathogen-associated molecular patterns (PAMPs) and damage-associated molecular patterns (DAMPs). PAMPs become present when infection of foreign cell lysis releases these foreign molecules intrinsic to their structure into the circulation, whereas DAMPs arise when cellular injury occurs at rates that overwhelm local clearance mechanisms. Thus, generalized bacteremia, severe pneumonia (viral or bacterial), severe trauma with tissue injury, and pancreatitis all share common inflammatory activation pathways **(Annane et al., 2009).**

The following is partial list of the infectious causes of SIRS: bacterial sepsis, burn wound infections, candidiasis, cellulitis, cholecystitis, community-acquired pneumonia, diabetic foot infection, erysipelas, infective endocarditis, influenza, intra-abdominal infections (eg, diverticulitis, appendicitis(gas gangrene, meningitis, nosocomial pneumonia, pseudomembranous colitis, pyelonephritis, septic arthritis, toxic shock syndrome, urinary tract infections (male and female), **(Dremsizov et al., 2013).**

The following is a partial list of the noninfectious causes of SIRS: acute mesenteric ischemia, adrenal insufficiency, autoimmune disorders, burns, chemical aspiration, cirrhosis, cutaneous vasculitis, dehydration, drug reaction, electrical injuries, erythema multiforme, hemorrhagic shock, hematologic malignancy, intestinal perforation, medication side effect (eg, from theophylline(, myocardial infarction, pancreatitis, seizure, substance abuse - stimulants such as cocaine and amphetamines, surgical procedures, toxic epidermal necrolysis, transfusion reactions, upper gastrointestinal bleeding and vasculitis **(Thoeni, 2012).**