Evaluation of red cell distribution width (RDW) as a septic marker in comparison with clinical scores and C-reactive protein

Thesis

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Ali Ahmed Naga

Contents

List of Abbreviations

ACCP	: American College of Chest Physicians
ALT	: Alanine aminotransferase
ANOVA	: Analysis of variance
APACHE	: Acute Physiology Age and Chronic Health Examination
ARDS	: Acute respiratory distress syndrome
AST	: Aspartate aminotransferase
ATPs	: Adenosine triphosphates
ATS	: American Thoracic Society
AUCs	: The Areas Under the Curve
CBC	: Complete blood count
CI	: Cardiac index
CNS	: Central nervous system
CO2	: Carbon dioxide
CRP	: C-reactive protein
cvaCO2	: Central venous-to-arterial carbon dioxide
DIC	: Disseminated intravascular
ESICM	: European Society of Intensive Care Medicine
FE	: Fisher Exact test
FIO2	: Fraction of Inspired Oxygen
HMGB1	: High-mobility group box 1
I/R	: Ischemic/reperfusion
ICU	: Intensive care unit

IL : Interleukin

IV : Intravenous

LPS : Lipopolysaccharides

MAP : Mean arterial pressure

MC : Monte Carlo test

MCV : Mean corpuscular volume

MIF : Migration inhibitory factor

MODS : Multiple organ dysfunction syndrome

mvaCO2 : Mixed venous-to-arterial carbon dioxide

NPV : Negative predictive value

PAMP : Pathogen associated molecular patterns

PCT : Procalcitonin

PMNs : Polymorphonuclear cells

PPV : Positive predictive value

PRR : Pattern recognition receptors

RBCs : Red blood cells

RDW : Red blood cell distribution width

ROC : Reciever Operating Curve

RRT : renal replacement therapy

rs : Spearman coefficient

SaO2 : Arterial oxygen saturation

SAPS : Simplified Acute Physiology Score

SCCM : Society of Critical Care Medicine

ScvO2 : Central venous oxygen saturation

SD : Standard deviation

NK : natural killer

SIRS : Systemic inflammatory response syndrome

SIS : Surgical Infection Society

SOFA : Sequential Organ Failure Assessment

T : Student t-test

TNF : Tumor necrosis factor

TLR : Toll – like receptors

UG : Ungraded

X2 : Chi Square test

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Introduction

Severe sepsis is the most common cause of death for patients admitted to the critical care units ***(Farag et al., 2013)***.

Sepsis is a multifaceted host response to an infecting pathogen that may be significantly amplified by endogenous factors ***(Wiersinga et al., 2014)***. Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection. This emphasizes the primacy of the non-homeostatic host-response to infection, the potential lethality that is considerably in excess of a straightforward infection, and the need for urgent recognition ***(Singer et al., 2016)***.

Sepsis, the inflammatory response to infection, affects millions of patients worldwide. However, its effect on overall hospital mortality has not been measured ***(Liu et al., 2013)***.

Sepsis, a syndrome of physiologic, pathologic, and biochemical abnormalities induced by infection, is a major public health concern in USA. The reported incidence of sepsis is increasing ***(Gaieski et al., 2013)***, likely reflecting

aging populations with more co-morbidities, greater recognition ***(Dellinger et al., 2013)***. Although the true incidence is unknown, conservative estimates indicate that sepsis is a leading cause of mortality and critical illness worldwide ***(Fleischmann et al., 2015)***.

Severity of organ dysfunction has been assessed with various scoring systems that quantify abnormalities according to clinical findings, laboratory data, or therapeutic interventions. The predominant score in current use is the Sequential Organ Failure Assessment (SOFA) ***(Kaukonen et al., 2015)***.

Nonspecific Systemic inflammatory response syndrome (SIRS) criteria such as pyrexia or neutrophilia will continue to aid in the general diagnosis of infection. These findings complement features of specific infections (e.g.; rash, lung consolidation, dysuria, peritonitis) that focus attention toward the likely anatomical source and infecting organism. Sepsis involves organ dysfunction, indicating a pathobiology more complex than infection plus an accompanying inflammatory response alone ***(Cecconi et al., 2014)***.

Early recognition of sepsis is not always straightforward and clinical signs at presentation can be misleading and very heterogeneous due to frequent comorbidities. In the emergency setting therefore an urgent need for a reliable diagnostic procedure, allowing early discrimination between SIRS and sepsis, is mandatory. Biomarkers, such as C-reactive protein (CRP) and procalcitonin (PCT), introduced among the diagnostic criteria of sepsis ***(Dellinger et al., 2013)***, could contribute to promptly identify patients affected by sepsis, severe sepsis and septic shock who could benefit from quick and appropriate therapy. C-reactive protein is one of the commonest biomarkers that are used during the management of sepsis. It was seen by some researchers to be significantly higher in sepsis patients compared to non-infectious SIRS ***(El-Shafie et al., 2017)***.

C-reactive protein production is a part of a larger picture of the acute phase response. This is principally regulated by the cytokines IL-6, Tumor necrosis factor alpha (TNF-α), and IL-1β are also regulatory mediators of CRP synthesis. C-reactive protein is directly involved in clearance of microorganisms. It causes activation of

neutrophils and enhances natural killer (NK) cell activity ***(Farag et al., 2013)***.

Inflammatory biomarkers commonly used in clinical practice (CRP) are influenced by nonspecific systemic inflammatory responses, which are mediated by the innate immune response. Therefore, it is recommended that multiple biomarkers should be evaluated simultaneously (multimarker strategy) and that plasma concentrations of these biomarkers should be determined repeatedly. Many potential biomarkers have been tested as diagnostic and prognostic tools for the management of antimicrobial therapy in septic patients ***(Franeková et al., 2017)***.

Aim of the Work

The aim of our study is to evaluate the level of RDW, CRP and clinical scores "SOFA and APACHI" as markers in patients with sepsis and their levels on the outcome and resolution of sepsis in ICU.