Red Cell Distribution Width versus Procalcitonin as a Marker for Severe Sepsis

Thesis

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Ahmed Atef Nagy El Desoki

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List of Abbreviations

Abb.	Full term
AP-1	*Activator protein 1*
APACHE II	*Acute Physiology, Age, Chronic Health Evaluation II*
CBC	*Complete blood count*
CGRP	*Glucocorticoid, calcitonin gene-related peptide*
CT	*Calcitonin*
CVP	*Central venous pressure*
DAMPs	*Damage-associated molecular patterns*
DNA	*Deoxyribonucleic acid*
ELISA	*Enzyme-linked immunosorbent assay*
ESI MS	*Electrospray ionized mass spectroscopy*
GCS	*Glasgow Coma Scale*
HIV/AIDS	*Human Immunodeficiency Virus/ Acquired Immune Deficiency Syndrome*
ICUs	*Intensive care units*
IL-6	*Interleukin-6*
LPS	*Lipopolysaccharide*
MAP	*Mean arterial pressure*
MCV	*Mean corpuscular volume*
MODS	*Multiple organ dysfunction syndrome*
mRNA	*Messenger Ribonucleic acid*
NO	*Nitric oxide*
PAMPs	*Pathogen-associated molecular patterns*

List of Abbreviations cont...

Abb.	Full term
PCR	*Polymerase chain reaction*
PCT	*Procalcitonin*
PRRs	*Pathogen-recognition receptors*
qSOFA	*Quick sequential organ failure assessment score*
RDW	*Red blood cell distribution width*
SBP	*Systolic blood pressure*
SIRS	*Systemic inflammatory response syndrome*
SOAP	*Sepsis Occurrence in Acutely Ill Patients*
SOFA	*Sequential Organ Failure Assessment*
SSC	*Surviving Sepsis Campaign*
TNF-α	*Tumor Necrosis Factor*
WBC	*White blood cells*

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INTRODUCTION

Severe sepsis and septic shock are major healthcare problems, affecting millions of individuals around worldwide each year, killing one in four (and often more), and increasing in incidence ***(Annane et al., 2005).***

It is very important that clinicians have the tools to identify and diagnose sepsis promptly because early diagnosis and treatment may lead to improvement in both mortality and morbidity. Gold standards for the diagnosis of infection do not exist, but procalcitonin is known to be among the most promising sepsis markers in critically ill patients, can complement clinical signs and routine laboratory variables that are suggestive of sepsis ***(Tang et al., 2007).***

The use of procalcitonin in developing countries such as Egypt, however, remains very expensive and hardly accessible in all ICUs. The red blood cell distribution width (RDW) represents an index of the heterogeneity of the erythrocytes (anisocytosis), which is calculated by dividing the standard deviation of erythrocyte volume by the mean corpuscular volume and multiplying by 100 to express the result as a percentage ***(Morris et al., 2001).***

AIM OF THE WORK

The aim of the study was evaluation the red cell distribution width as a prognostic marker of sepsis and as a predictor of mortality compared with procalcitonin.

REVIEW OF LITERATURE

Sepsis and Septic Shock

Incidence:

The global epidemiological onus of sepsis is difficult to ascertain. It is estimated to affect more than 30 million people worldwide every year, potentially leading to 6 million deaths ***(Fleischmann et al., 2016).***

The true incidence of sepsis in any given country is unknown. The reported incidence is dependent on the specific definition used, the infecting organism, the reporting mechanism and the requirement for either organ support or intensive care. These factors result in marked differences between estimates and discrete geographical locations. Most data describing the incidence of sepsis are from high-income countries, where 2·8 million deaths per year are attributable to sepsis ***(Adhikari et al., 2010).***

Sepsis is one of the most prevalent causes of mortality in intensive care units (ICUs), and its incidence increased by more than double over the last 10 years ***(Kumar et al., 2011).***

Definitions:

Older definitions

A 1991 consensus conference developed initial definitions that focused on the then-prevailing view that:

Sepsis 1 resulted from a host's systemic inflammatory response syndrome (SIRS) to infection **(table 1).** Sepsis complicated by organ dysfunction was termed severe sepsis, which could progress to septic shock, defined as "sepsis-induced hypotension persisting despite adequate fluid resuscitation." ***(Bone et al., 1992).***

Table 1: Diagnostic criteria of SIRS (**sepsis 1)** ***(Bone et al., 1992)***

SIRS (systemic inflammatory response syndrome) two or more of:
• Temperature >38°C or <36°C
• Heart rate >90/min
• Respiratory rate >20/min or PaCO2 <32 mm Hg (4.3 kPa)
• White blood cell count >12000/mm3 or <4000/mm3 or >10% immature bands

Sepsis 2: A second international sepsis definitions conference was convened in 2001, and the results were published in 2003. The 2001 consensus retained the definitions of sepsis as SIRS due to infection (presumed or confirmed) and severe sepsis as sepsis associated with acute organ dysfunction **(table 2)**

Table 2: Diagnostic criteria of sepsis **(sepsis 2)** ***(Gül et al., 2017)***

Diagnostic criteria for sepsis
Infection
Documented or suspected and some of the following:
General parameters
Fever (core temperature >38.3°C)
Hypothermia (core temperature <36°C
Heart rate > 90 bpm or > 2 SD above the normal value for age
Tachypnea: >30 bpm
Altered mental status
Significant edema or positive fluid balance (>20 mL kg^{-1}over 24 h)
Hyperglycemia (plasma glucose >110 mg dL^{-1} or 7.7 mM L^{-1}) in the absence of diabetes
Inflammatory parameters
Leukocytosis (white blood cell count >12, 000/μL)
Leukopenia (white blood cell count <4, 000/μL)
Normal white blood cell count with >10% immature forms Plasma C reactive protein >2 SD above the normal value Plasma procalcitonin >2 SD above the normal value
Hemodynamic parameters
Arterial hypotension (systolic blood pressure <90 mmHg, mean arterial pressure <70, or a systolic blood pressure decrease >40 mmHg in adults or <2 SD below normal for age)
Mixed venous oxygen saturation >70% Cardiac index >3.5 l min^{-1} m^{-2}
Organ dysfunction parameters
Arterial hypoxemia (PaO_2/FiO_2 <300)
Acute oliguria (urine output <0.5 ml kg^{-1} h^{-1} or 45 mM L^{-1} for at least 2 h) Creatinine increase ≥0.5 mg dL^{-1}
Coagulation abnormalities (international normalized ratio >1.5 or activated partial thromboplastin time >60 s)
Ileus (absent bowel sounds)
Thrombocytopenia (platelet count <100, 000/μL)
Hyperbilirubinemia (plasma total bilirubin >4 mg dL^{-1} or 70 mmol L^{-1})
Tissue perfusion parameters
Hyperlactatemia (>3 mmol L^{-1})
Decreased capillary refill or mottling

Newer definitions

Sepsis 3: According to the third international consensus of definition of sepsis and septic shock (2016).

Sepsis is a life threatening organ dysfunction due to a dysregulated host response to infection

Sepsis clinical criteria: organ dysfunction is defined as an increase of 2 points or more in the Sequential Organ Failure Assessment (SOFA) SCORE **(Table 3).**

* For patients with infections, an increase Of 2 SOFA points gives an overall mortality rate of 10 %

(Vincent et al., 1998)

A higher SOFA score is associated with an increased probability of mortality ***(Vincent et al., 1998).***

The score grades abnormality by organ system and accounts for clinical interventions. However, laboratory variables, namely, PaO2, platelet count, creatinine level, and bilirubin level, are needed for full computation. Furthermore, selection of variables and cutoff values were developed by consensus, and SOFA is not well known outside the critical care community. Other organ failure scoring systems exist, including systems built from statistical models, but none are in common use ***(Vincent et al., 2014).***