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# Role of Troponin-T at Admission and Serial Troponin-T Testing in Predicting Outcomes in Severe Sepsis and Septic Shock

*Thesis*

***Submitted for Partial Fulfillment of Master Degree in Intensive Care Medicine***

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### *Before all thanks to Allah*

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# List of Abbreviations

| Abb. | Full term |
|---|---|
| **AKI** | Acute kidney injury. |
| **ALT** | Alanine aminotransferase |
| **APACHE** | Acute Physiology, Age, Chronic Health Evaluation |
| **aPTT** | Activated partial thromboplastin time |
| **ARDS** | Acute respiratory distress syndrome |
| **AST** | Aspartate aminotransferase |
| **CARS** | compensatory anti-inflammatory syndrome |
| **CD4** | Cluster of differentiation 4 |
| **CRP** | C-reactive protein |
| **CT** | Computed tomography |
| **cTn** | Cardiac troponin |
| **CVP** | Central venous pressure |
| **CXR** | Chest X- ray |
| **DAD** | Diffuse alveolar damage |
| **DIC** | Disseminated intravascular coagulopathy |
| **ECG** | Electrocardiogram |
| **ED** | Emergency department |
| **FDA** | Food and drug administration |
| **GCSF** | Granulocyte colony stimulating factor |
| **GM-CSF** | Granulocyte-macrophage colony-stimulating factor |
| **HCT** | Hematocrite |

| Abb. | Full term |
|---|---|
| **H-FABP** | Heart-type fatty acid-binding protein |
| **HLA** | Human leucocytic |
| **HR** | antigen |
| **hs-cTnT** | Heart rate |
| **ICU** | High sensitive cardiac troponin T |
| **IgG** | Intensive care unit |
| **IHD** | Immunoglobulin G |
| **IL** | Ischemic heart disease |
| **IL-1** | Interleukin |
| **INR** | Interleukin-1 |
| **LBBB** | International normalized ratio |
| **LFABP** | Left bundle branch block |
| **LOS** | L-type fatty acid-binding protein |
| **LPS** | Length of stay |
| **LV** | lipopolysaccharides |
| **MAP** | Left ventricle |
| **MARS** | Mean arterial pressure |
| **MODS** | Mixed antagonistic response syndrome |
| **MV** | Multiorgan dysfunction syndrome |
| **NADPH** | Mechanical ventilation |
| **NETs** | Nicotinamide adenine dinucleotide phosphate |
| **NO** | Neutrophil extracellular |
| **NOS** | traps |
| **NSTEMI** | Nitric oxide |
| **PAMPs** | Nitric oxide synthase |

| Abb. | Full term |
|---|---|
| **PARs** | Non ST- elevation myocardial infarction |
| **PC** | Pathogen-associated molecular proteins |
| **PCT** | Protease-activated receptors |
| **PEEP** | Personal computer |
| **Pro ADM** | Procalcitonin |
| **qSOFA** | Positive end expiratory pressure |
| **RR** | Proadrenomedullin |
| **SAE** | Quick Sequential organ failure assessment |
| **SBP** | Respiratory rate |
| **SBP** | Sepsis associated encephalopathy |
| **ScvO2** | Systolic blood pressure |
| **SD** | Systolic blood pressure |
| **SIRS** | Venous oxygen saturation |
| **SOFA** | Standard deviation |
| **SPSS** | Systemic inflammatory response syndrome |
| **STEMI** | Sequential organ failure assessment |
| **TLC** | Statistical Package for the Social Sciences |
| **TLRs** | ST- elevation myocardial infarction |
| **TNF** | Total leucocytic count |
| **TNFα** | Toll-like receptors |
| **TTE** | Tumor necrosis factor |
| **URL** | Tumor necrosis factor alpha |
| **WBC** | Transthoracic echocardiography |

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# Abstract

**Background:** Serum troponin concentrations have been associated with increased mortality in almost every clinical setting they have been examined, including sepsis. Sepsis is the physiological response to severe infection. It is defined as the presence (probable or documented) of infection together with systemic features of inflammation. Severe sepsis is sepsis-induced tissue hypoperfusion or organ dysfunction, and septic shock refers to sepsis-induced hypotension, persisting despite adequate fluid resuscitation, which may be defined as infusion of 30 ml/kg of crystalloids. Elevated troponin levels are observed in 43% across all intensive care patient groups. The estimated prevalence of positive troponin in the context of sepsis is 61%. The mechanism of myocyte insult in severe sepsis and septic shock, in the absence of thrombotic acute coronary syndrome, leading to elevated serum troponin, is not yet fully understood. Myocardial depressive factors (inflammatory mediators, endotoxins), microvascular dysfunction and increased myocardial cell membrane permeability in conjunction with myocardial oxygen demand– supply mismatch, are potential explanations for sepsis induced troponin elevation. In this setting, troponin elevation occurs in the absence of myocytenecrosis and this hypothesis is supported by clinical observations that myocardial depression in the context of sepsis is a reversible process in most surviving patients. The aim of this study is to evaluate the prognostic value of troponin T level at admission and serial troponin T testing in patients with severe sepsis and septic shock. This work was carried on 70 patients with severe sepsis and septic shock from those attending the intensive care units in Ain shams university hospitals in the time period between February 2018 and July 2018. These patients were subdivided into 2 groups each consisted of 35 patients, the first group with elevated troponin T at admission and the other group with negative troponin T at admission.

**Keywords:** Role; Troponin-T; Admission; Serial Troponin-T; Testing; Predicting Outcome; Severe Sepsis; Septic Shock

# Introduction

Sepsis is a leading cause of death and disability worldwide, resulting in a huge number of fatalities as acute myocardial infarction (AMI) each year **(Bessiere et al., 2013)**. Cardiovascular dysfunction occurs in nearly 70% of septic patients and can manifest as hemodynamic instability, cardiac biomarker elevation, myocardial dysfunction on echocardiography, and end-organ hypoperfusion **(Antonucci et al., 2014)**. Cardiovascular dysfunction in sepsis is associated with worse hospital and long-term outcomes, necessitating early diagnosis and management **(Angus et al., 2001)**.

Cardiac troponin-T (TnT) and troponin-I (TnI) are sensitive and specific markers of myocardial injury and have prognostic implications in many primary non cardiac illnesses including pulmonary embolism, subarachnoid hemorrhage, and stroke **(Jimenez et al., 2009)**. Increased sensitivity of the TnT assay has resulted in more frequent clinical detection of myocardial injury from non-coronary causes, including critical illness **(Newby et al., 2012)**. Elevations in TnT levels are present in up to 60% of all intensive care unit (ICU) patients and identify patients with

increased risk of short-term and long-term mortality **(Babuin et al., 2008)**.

Up to 85% of patients with sepsis and septic shock have detectable cardiac TnT levels using standard troponin assays, and troponin levels have demonstrated a variable association with mortality **(Ammann et al., 2001)**. Cardiac TnT levels correlate with the presence of left ventricular systolic and diastolic dysfunction and right ventricular dysfunction on echocardiography **(Klouche et al., 2014)**. TnT levels in patients with sepsis correlate with duration of hypotension and extent of vasopressor support **(Chelazzi et al., 2011)**. Prior studies evaluating the role of troponins in sepsis and septic shock were limited by the use of different troponin assays, small sample sizes, variations in definitions of elevated troponin levels, and loss of patients to follow-up **(Bessiere et al., 2013)**. These studies display marked heterogeneity because of lack of uniform adaptation of the 99th percentile of the upper reference limit as the standardized cutoffs **(Pulkki et al., 2009)**. Thus, the epidemiology and prognostic value of troponin levels in patients with sepsis depend not only on the assay used but also on the cutoff values used.

# Aim of the Work

The aim of this study is to evaluate the prognostic value of TnT in patients with severe sepsis and septic shock. The outcome will be in-hospital mortality, need for mechanical ventilation, the need for vasopressors and length of ICU stay.

**Chapter** (1):

# Definition, Pathophysiology and Management of Sepsis

The term sepsis is derived from a Greek word meaning "putrid". It was believed that putrefaction of a wound was caused by contact with air and that death occurred when the process of putrefaction reached the blood (septicemia). In the 19th century, the concept of infection as a cause of sepsis was introduced by the Austrian obstetrician, *Ignaz Philipp Semmelweis* and the English surgeon, *Joseph Lister* ***(Vincent, 2011)***. From then on, the term sepsis was closely connected to bacterial infection. However, as the understanding of human immune physiology improved, the importance of the host response to infection in the pathophysiology of sepsis was recognized ***(Vincent, 2011)***.

## Definitions

A 1991 consensus conference developed initial definitions that focused on view that sepsis resulted from a host's systemic inflammatory response syndrome (SIRS) to infection. 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". A 2001 task force, recognizing limitations with these definitions, expanded the list of diagnostic criteria but did not offer alternatives because of the lack of supporting evidence ***(Levy et al., 2003).***

## Surviving Sepsis Campaign 2012

The Surviving Sepsis Campaign has attempted to increase awareness and establish practice guidelines to improve the recognition and treatment of patients with severe sepsis and septic shock. Several studies of the initial assessment and management of the emergency department (ED) patient with severe sepsis and septic shock have been published. The results of these studies were incorporated into the newly published 2012 Surviving Sepsis Campaign Guidelines ***(Dellinger et al., 2013).***

Sepsis is defined as probable (documented or suspected) infection and signs of systemic inflammation. Severe sepsis is defined as sepsis and organ dysfunction or tissue hypoperfusion.

Septic shock is defined as sepsis induced hypotension despite adequate fluid resuscitation (table 1).