Increased Body Mass Index and Adjusted Mortality in Intensive Care Unit Patients with Sepsis or Septic Shock.

Thesis

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List of Abbreviations

Abbr.	Full term
AgRP :	Agouti-related peptide
AKI :	Acute kidney injury
APACHE:	Acute Physiology, and Chronic Health Evaluation
ARDS:	Acute respiratory distress syndrome
AT:	Antithrombin
ATP:	Adenosine triphosphate–sensitive potassium
ATS:	American Thoracic Society
BMI:	Body mass index
CART :	Cocaine- and amphetamine-regulated transcript
COPD:	Chronic obstructive pulmonary disease
CRP :	C-reactive protein
DAD:	Diffuse alveolar damage
DIC:	Disseminated intravascular coagulopathy
ED:	Emergency department
ESICM:	European Society of Intensive Care Medicine
FTO gene:	Fat mass and obesity associated gene
GCSF :	Granulocyte colony stimulating factor
GM-CSF:	Granulocyte-macrophage colony-stimulating factor
HCT :	Hematocrite
ICU:	Intensive care unit
IL-1:	Interleukin 1
LH:	lateral hypothalamus
LV :	Left ventricular

MAP:	Mean arterial pressure
MODS:	Multiorgan dysfunction syndrome
NETs :	Neutrophil extracellular traps
NIH :	National Institutes of Health
NOS:	Nitric oxide synthase
NPY :	Neuropeptide Y
PAD:	Peripheral artery disease .
PAMPs:	Pathogen-associated molecular proteins
PARs :	Protease-activated receptors
POMC:	Pro-opiomelanocortin
qSOFA:	quick sequential organ failure assessment
SAE :	Sepsis associated encephalopathy
SBP :	Systolic blood pressure
SD:	Standard deviation
SIRS:	Systemic inflammatory response syndrome
SIS:	Surgical Infection Society
SOFA:	Sequential organ failure assessment
SSC:	Surviving Sepsis Campaign
TLRs:	Toll-like receptor family
TNF:	Tumor necrosis factor
TNFα :	Tumor necrosis factor alpha
UOP:	Urine output
VMH:	Ventromedial hypothalamus
WBC:	White blood cells
WHO:	World Health Organization

Abstract

Sepsis is life - threatening organ dysfunction caused by a dysregulated host response to infection and is characterized by the presence of suspected or proven infection accompanied by an increase in sequential (sepsis - related) organ failure assessment (SOFA) score of two points or more from baseline. Sepsis is one of the most common causes of death among hospitalized patients in the intensive care unit (ICU). It is particularly difficult to diagnose in this setting because of the multiple comorbidities and underlying diseases that these patients present. Over the past few decades, a growing body of evidence has investigated the values of different predictors of sepsis-related mortality. Previously, it was reported that old age, tachycardia, hypotension, elevated C-reactive protein (CRP) and lactate, thrombocytopenia, need of mechanical ventilation, high Acute Physiology, and Chronic Health Evaluation (APACHE) II, and high SOFA scores were variables associated with high mortality. Recently, a growing number of published studies have reported that obesity can be significantly correlate with mortality in the ICU setting. Body mass index (BMI) is one of the common clinical demographic characteristics and can be calculated from the ratio of body weight to squared height (kg/m^2). Nevertheless, data are limited regarding the role of BMI in predicting short-term mortality among patients with sepsis. Therefore, we conducted the present prospective study in order to evaluate the effect of increased BMI on mortality in ICU patients with sepsis or septic shock. The present study included 45 adult patients (≥16 years old) who were admitted to the ICU and treated for sepsis, severe sepsis, or septic shock. The patients were divided into three groups based on their BMI. In the present study, the average age of the included patients ranged from 55-70 years old; while the majority of patients were males. Moreover, we found that patients with a BMI < 25kg/m2 were older than other groups of patients. On the other hand, patients with BMI > 30kg/m2 were more likely to have diabetes mellitus. Regarding the cause of admission, our analysis showed that patients with low BMI (< 25 kg/m2) were more likely to have chest infection; while patients with high BMI (>30 kg/m2) were more likely to have bed sores. In terms of vital signs of the included patients during the first day of admission, the present study shows that obese patients had significantly lower body temperature, heart rate, and respiratory rates; while they had significantly higher mean arterial blood pressure than patients in other BMI groups. Our analysis showed that the mortality rate was significantly lower in obese patients than other BMI groups ($p = 0.049$). On the other hand, there were no significant associations between BMI and ICU length of stay, APACHE II Score, SOFA score, or rate of readmission. In concusion, Obesity is a potential predictive characteristics for mortality among septic patients admitted to ICU.

Keywords: Body Mass; Index; Adjusted Mortality; Intensive Care Unit; Patients; Sepsis; Septic Shock

INTRODUCTION

BMI is a value derived from the mass (weight) and height of an individual. The BMI is defined as the body mass divided by the square of the body height, and is universally expressed in units of kg/m2, resulting from mass in kilograms and height in metres. - **Sepsis** is life-threatening organ dysfunction caused by a dysregulated host response to infection.

Septic shock is subset of sepsis in which circulatory, cellular, and metabolic abnormalities are associated with a greater risk of mortality than with sepsis alone . Over the last few decades, obesity has emerged as an international public health problem and is a leading cause of preventable deaths. The World Health Organization estimated in 2008 that 11% of adults aged 20 years and older were obese (body mass index [BMI] > 30kg/m2) . This is of particular concern because obesity is associated with a heightened risk of morbidity and mortality from many acute and chronic medical conditions ***(Honiden S, McArdle JR 2009).***

Furthermore, the prevalence of obesity is increasing across the globe , a finding that has major implications for healthcare planners and policy makers when considering

appropriate allocation of resources. Obese individuals have a greater burden of comorbid conditions than their non-obese counterparts. They also are more likely to develop physiologic derangements and have diminished physiologic reserve available to compensate for the stress of critical illness **.** ***(Porhomayon J et al ., 2014)***

Despite these factors, investigations have been unable to conclusively demonstrate an adverse effect of obesity on outcomes from critical illness .In fact, some have suggested a protective effect of obesity, a phenomenon termed the obesity-survival paradox ***(Pickkers P et al ., 2013)***

Similarly, although some studies have reported an increased risk of acquiring denovo infection in obese patients admitted to the ICU **,** others were unable to validate this finding **„**In studies of adults admitted to the ICU with sepsis, severe sepsis, or septic shock and which adjusted for other baseline variables, patients with overweight or obese BMIs, but not morbidly obese ones, had reductions in mortality at up to 28 days compared to those with normal BMIs. There are several plausible biologic and physiologic reasons for these mortality reductions with the two former categories. First, increased adipose tissue is associated with increased renin-angiotensin system activity (***Kershaw EE, Flier JS***

2004). While this increased activity contributes to the hypertension of overweight and obese patients, it could also have protective hemodynamic effects during sepsis and decreased the need for fluid or vasopressor support, therapies which in excess can adversely impact outcome. ***(Yealy DM et al. , 2014)*** , increased lipoprotein levels and adipose tissue in patients with increased BMI may bind and inactivate lipopolysaccharide or other harmful bacterial products released during sepsis .

Third, excess adipose tissue could provide increased beneficial energy stores during the catabolic septic state ***(Thompson PA, Kitchens RL 2006)***

. Finally, excess adipose tissue may have beneficial immune functions. For example, adipose tissue has been associated with increased production of both tumor necrosis factor (TNF) and soluble TNF receptor ,,Studies have suggested that obesity suppresses injurious inflammatory mediator release during sepsis and sepsis-associated acute lung injury . ***(Stapleton RD, Suratt BT 2014)***

AIM OF THE WORK

Perform a systematic review of adjusted all-cause mortality for overweight, obese relative to normal BMI for adults admitted to the ICU with sepsis, severe sepsis, and septic shock.