Caring for the Critically Ill Obese Patient: Challenges and Opportunities

Robert D. Winfield, MD

Abstract
Obesity remains a challenging public health problem. The anatomic and physiologic complexities of obese patients make their healthcare challenging under routine circumstances, but in the setting of critical illness, these challenges are magnified. This review explores some of the unique difficulties that critical care providers face when caring for the obese patient and highlights areas in which future research is needed to provide optimal care. (Nutr Clin Pract. XXXX;xx:xx-xx)

Keywords
obesity; critical illness; intensive care

Obesity is a complex disease state most readily characterized by the presence of excess adipose tissue and is among the most pressing worldwide public health issues of the 21st century. Worldwide, there are >500 million obese adults,1 with most of these individuals in the developed world. However, overall, obesity rates have been steadily increasing in recent years, even in second- and third-world economies.1 There are a variety of methods for determining one’s level of body fat, but from the standpoint of simplicity (and hence usability in epidemiologic research), body mass index (BMI) has gained the widest acceptance. BMI is calculated by a simple formula (Table 1), and the World Health Organization1 classifies individuals as obese once BMI reaches 30 kg/m². As obesity rates increase, the impact on the healthcare system is broad, and in no setting is an understanding of the unique pathophysiology and characteristics of the obese patient more important than the realm of critical care. This article will review some of the significant features of obesity that affect management in the intensive care unit and some potential ways that these conditions might be managed in the future.

The Conundrum of Cardiovascular Dysfunction in the Critically Ill Obese Patient

The obese individual exists in a variable and complex state of pathophysiology that touches nearly all major organ systems. Cardiovascular disease is perhaps the condition most commonly associated with obesity, as there are well-recognized and established links between obesity and atherosclerotic cardiac and vascular disease2 with associated risk of hypertension and stroke. This predilection for vascular dysfunction may lead to the development of the “obesity cardiomyopathy” syndrome, characterized initially by ventricular hypertrophy and increased systemic vascular resistance followed by a gradually developing dilated cardiomyopathy.3 Although less common, obese patients are also at risk for a peculiar restrictive cardiomyopathy characterized by fatty infiltration of the myocardium known as adipositas cordis.4

To complicate matters, hemodynamic monitoring can be a major challenge in the obese patient. Umana et al5 compared patients of varying BMI groups on the basis of correlation between noninvasive and invasive blood pressure monitoring. They found that as BMI class increased, the correlation between cuff measurements and direct measurement with an arterial line worsened. The tendency in the patients studied was for blood pressure cuffs to underestimate systolic blood pressure and overestimate diastolic blood pressure. Other standard methods are also unreliable in the obese. Among critically ill patients who sustained severe blunt trauma, central venous pressure measurements correlated only with BMI class and not resuscitative adequacy, as measured by slower resolution of base deficit (a surrogate measure of the amount of volume resuscitation estimated to restore tissue perfusion and correct systemic acidosis) in morbidly obese patients.6 The inadequacies of current hemodynamic monitoring can have adverse consequences that should prompt caution in the administration of enteral nutrition supplementation, as they can either suggest instability that does not exist or seeming stability in a patient

From 1Department of Surgery, Section of Acute and Critical Care Surgery, Washington University School of Medicine, St Louis, Missouri.

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Corresponding Author:
Robert D. Winfield, MD, Department of Surgery, Section of Acute and Critical Care Surgery, Washington University School of Medicine, 660 S Euclid Avenue, Mail Code 8109, St Louis, MO 63110, USA.
Email: winfieldr@wudosis.wustl.edu.
resuscitated to a suboptimal degree. In the former scenario, nutrition supplementation may be unnecessarily delayed; in the latter, adverse consequences such as nonocclusive mesenteric ischemia may be triggered.7

The optimal method for determining the cardiovascular state of the obese patient and monitoring the sufficiency of resuscitation has yet to be determined. What is clear is that standard approaches will likely not work beyond the most straightforward of situations. As such, alternative methods should be considered when any doubt exists as to the validity of measurement. An arterial line should be used in any scenario in which blood pressure falls outside of the anticipated range in an obese patient, particularly where hypotension is encountered. Depending on the scenario and the comfort level of the practitioner, a variety of methods may be used to evaluate cardiovascular function and resuscitation. These may include transesophageal echocardiography, which can aid in identifying myocardial abnormalities as well as ventricular filling; serial measurement of central venous oxygen saturation in a patient requiring ongoing resuscitation; so-called minimally invasive hemodynamic monitoring, which can provide a variety of data regarding cardiac and vascular function; and perhaps pulmonary artery catheters may have a role in these challenging patients.8 It is important to recognize that none of these has been specifically studied and shown to improve outcome in the critically ill obese patient; however, given the inherent challenges in hemodynamic monitoring, the more detailed level of data that can be obtained from these technologies may prove invaluable for the intensivist. Ultimately, comparison of these methods may help guide their use in the care of the obese.

Can Endocrine Management be Improved in the Critically Ill Obese?

If cardiovascular disease is not the most significant comorbidity seen in the obese, then endocrine dysfunction likely is. Obesity is strongly linked with the development of insulin resistance and type 2 diabetes and, further, with hypothalamic and pituitary dysfunction that lead to elevated cortisol levels and exacerbation of insulin resistance.9 The pathophysiology of adipose tissue–mediated insulin resistance was elucidated by Hotamisligil et al10 in 1993. This group of investigators demonstrated conclusively that adipose tissue–derived tumor necrosis factor–alpha (TNF-α)–mediated inflammation was central to the process, and subsequent studies have confirmed the role of TNF-α and identified other adipose-derived mediators that play a role in the development of insulin resistance.11 Adipose-derived and adipose-converted angiotensin II in particular seem to play an important role in insulin resistance,12 and reversal of inflammation, insulin resistance, and metabolic dysfunction have been noted when angiotensin-converting enzyme inhibitors as well as angiotensin receptor blockers are administered to obese patients.13,14

From a practical standpoint, obese patients in the intensive care unit have greater daily insulin requirements to maintain reasonable control of blood glucose levels,15 and achieving this control without the risk of hypoglycemia can be challenging.16 Looking ahead to methods and technology that may assist with this difficult problem, an answer may come from new equipment that permits continuous blood glucose monitoring. At present, several monitoring systems are being developed and validated in the setting of critical illness and offer the promise of tight control without hypoglycemia.17,18 While this will likely be of value to many patients in the intensive care unit, given their underlying predilection for endocrine dysfunction, the obese may be the primary beneficiaries of this new technology.

Preventing Venous Thromboembolic Disease in the Obese ICU Patient

Obesity is a hypercoagulable state. This results from a combination of causes, including adipose tissue production of the procoagulants tissue factor and plasminogen activation inhibitor–1,19 as well as intrinsic platelet dysfunction characterized by hyperactivity and resistance to anticoagulant stimuli.20 This partially explains the elevated risk of myocardial infarction in critically injured obese patients2 and the heightened risk of cerebrovascular accidents.21 In addition, the combination of this hypercoagulable state with post-illness debility and the greater challenges associated with mobilizing the heavier patient create the perfect storm, in which the obese patient is at heightened risk for venous thromboembolic disease such as deep vein thrombosis and pulmonary embolism. While this is a well-recognized risk in the obese, data are lacking on optimal methods for the prevention of this complication.22 A variety of methods has been proposed, including low-dose heparin infusions, weight-based intermittent dosing of low-molecular-weight and unfractionated heparin, and alternative agents such as fondaparinux; however, most of these have not been studied in a rigorous fashion or with appropriate power to draw adequate conclusions.23 As a result, this issue will likely be solved through well-designed trials that compare methods on the ability to achieve appropriate levels of anticoagulation using anti-Xa levels or thromboelastometry/thromboelastography and then follow this with a determination of whether or not this leads to a reduction in venous thromboembolic events.

### Table 1. Body Mass Index Classification.

<table>
<thead>
<tr>
<th>Classification</th>
<th>Body Mass Index (Weight in Kilograms/Height in Meters)²</th>
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<tbody>
<tr>
<td>Underweight</td>
<td>&lt;18.5</td>
</tr>
<tr>
<td>Normal</td>
<td>18.5–24.9</td>
</tr>
<tr>
<td>Overweight</td>
<td>25–29.9</td>
</tr>
<tr>
<td>Obese</td>
<td>30–39.9</td>
</tr>
<tr>
<td>Morbidly obese</td>
<td>≥40</td>
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Will Immune Modulation Lead to Better Outcomes Among the Obese?

Obesity is a disease of immune dysfunction. Obese patients are commonly believed to exist in a baseline proinflammatory state, and when traditional systemic markers of inflammation such as total white blood cell count and C-reactive protein concentration are considered, this inflammatory condition is confirmed by baseline elevation in these markers in obese relative to lean patients. In addition, the balance of cytokines and adipose-derived mediators of inflammation (adipokines) suggests a state of chronic inflammation. To refer to this as a pure state of immune activation would be an oversimplification, however. While adipose tissue macrophages and pulmonary alveolar macrophages appear to be in a proinflammatory mode, there are other changes in immune function that suggest an impaired immune response. Sheridan et al demonstrated that obese patients exposed to influenza vaccine had a more robust initial response, as noted by elevated IgG levels; however, at 12 months, lower influenza antibody titers and a decreased responsiveness of peripheral blood mononuclear cells to influenza challenge were observed in obese patients compared with lean patients. In critically ill blunt trauma patients, both pro- and anti-inflammatory cytokine concentrations were suppressed in the first 4 days following injury, suggesting a blunting of immune response in this early time period; this was associated with a greater incidence of nosocomial infection and later onset of multiple organ failure, the latter perhaps owing to the former.

Can Immunonutrition Affect Outcomes in the Critically Ill Obese Patient?

The relationship between obesity, nutrition, and outcome in the obese patient is extremely complex. As previously mentioned, adipose-derived TNF-α and other mediators lead to the development of insulin resistance and diabetes mellitus, but the inflammatory changes brought on by obesity have further-reaching consequences on global metabolism. Obesity can be associated with a paradoxic state known as “sarcopenic obesity,” wherein the inflammation of obesity leads to a reduction in muscle mass, which leads to muscle weakness and decreased mobility, which then exacerbates the accumulation of adipose tissue, feeding into a cycle of increasing inflammation and mobility, which then exacerbates the accumulation of adipose in muscle mass, which leads to muscle weakness and decreased density,” wherein the inflammation of obesity leads to a reduction in muscle mass will result in worsened muscle weakness, decreased mobility, and prolonged recovery. As a result, the American Society for Parenteral and Enteral Nutrition guidelines suggest the use of early administration of hypocaloric, high-protein nutrition. Once again, the true beneficial effect of this practice is unclear, as clinical data are limited to only a small series and in aggregate fail to demonstrate superiority, but the data on which the guideline is based indicate an improved nutrition profile that should prove beneficial and may improve functional recovery as well as inflammatory profile.

At this point, the relationship between immune dysfunction and outcome in the critically ill obese patient is poorly understood, but with a better understanding of cell-specific function in the settings of critical illness or severe injury, it is conceivable that immune modulation, whether through immunonutrition, targeted immune adjuvants, or medications with more global immune regulatory activities, may help to decrease the rates of complications in the critically ill obese patient and improve outcomes.

Summary

Obesity represents a daunting problem for critical care providers, both in the increasing volume of patients with this condition and in the complexity of issues faced. At this point in time, the complex pathophysiology of the obese patient poses a major challenge for intensivists, as there are more questions than answers with regard to optimal management of these patients. The optimist sees in this that there are great opportunities to improve care and management of these patients through the development of obesity-specific care protocols and pathways and in unraveling the mystery of immune dysfunction in these physiologically and immunologically complex patients.

References


