The Critically Injured Obese Patient: A Review and a Look Ahead

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According to recent estimates, approximately 103 million adults in the United States, representing greater than one-third of the population, have a body mass index (BMI) greater than 30 kg/m², classifying them as obese.1 Worldwide, the number of obese adults is greater than 500 million, and these numbers continue to increase annually.2 In addition, the number of obese children and adolescents has risen dramatically in recent years, suggesting a future in which obesity rates will continue to rise.2 Obesity and its associated complications place substantial strain on the health care system, both logistically and financially. These patients consume more health care resources than patients of normal BMI, with Finkelstein and colleagues3 estimating that $147 billion dollars were spent in 2008 on obesity-related illness, and that the costs to third-party payors for obese patients were $1,429 higher per individual than for their normal BMI counterparts.

As the number of obese individuals increases, their presence will be felt in all areas of health care. With the particularly high increases seen in childhood and adolescent obesity, it is important to remember that despite the likelihood of developing obesity-associated diseases over the course of a lifetime, the leading cause of death and disability in this young patient group through their middle-age years remains traumatic injury.4 This combination of obesity and trauma will provide a series of novel challenges for those devoted to caring for the critically injured. In this review, we will evaluate the critically injured obese patient, beginning with a brief description of the disease summarizing the existing trauma and critical care literature and concluding with a look at the many questions that remain unanswered with regard to this pressing issue and potential directions for future investigation.

OBESITY AND ASSOCIATED HEALTH CONCERNS

Obesity is associated with a number of known health concerns that represent complex interactions between anatomy, physiology, and immune dysfunction (Fig. 1). These are considered systematically here to provide an understanding of the underlying conditions that may have an impact on the care of the injured obese patient.

Cardiac and vascular

Obesity has long been linked to cardiac and vascular dysfunction. The obese patient is known to have an increased risk of atherosclerotic cardiovascular disease.5 This is related to the presence of diabetes, hyperlipidemia, and an overall prothrombotic state, which accelerates and enhances the risk of vascular complications such as myocardial infarction and stroke.6-8 These same factors, along with endocrine dysfunction in blood pressure regulation, lead to an increased systemic vascular resistance and hypertension. Over the long term, this can promote the development of “obesity cardiomyopathy,” which is characterized by an initial left ventricular hypertrophy and diastolic dysfunction followed by dilated cardiomyopathy and systolic dysfunction.9 In addition, hyperlipidemia and associated lipotoxicity can actually lead to direct fatty infiltration of myocardium and a restrictive cardiomyopathy known as adipositas cordis.10,11

Pulmonary

Pulmonary dysfunction is also common in the obese patient. A number of studies have linked obesity with asthma, and it has been suggested, if not definitively proven, that this is related to chronic inflammation.12,13 Aside from airway reactivity though, the size and fat distribution of the obese patient is a prominent feature in obesity-related disease. Body mass index (BMI), visceral adipose tissue, and subcutaneous adipose tissue all affect pulmonary mechanics, with increases in these features corresponding with decreases in expiratory reserve volume, residual volume, and vital capacity.14 Approximately 10% to 20% of patients are presumed to have the obesity hypoventilation syndrome, in which baseline pCO₂ is greater than 45 mmHg and pO₂ is less than 75 mmHg.15 This is separate from, but similar to, the problem of obstructive sleep apnea, seen in up

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to 45% of the obese.\textsuperscript{16,17} Although likely multifactorial in nature, anatomic changes in obesity including deposition of fat in the visceral and soft tissues of the neck leading to diminution of airway size and increased collapsibility, which appear to play a key role in the disease process, and this may be remedied through the use of noninvasive positive pressure ventilation.\textsuperscript{17,18}

\textbf{Renal}

The renal system is also known to be dysfunctional in obese patients; with increases in BMI, the risk of development of chronic kidney disease and the need for dialysis increase in a linear fashion.\textsuperscript{19} Although the previously mentioned cardiovascular abnormalities of hypertension, atherosclerotic disease, and cardiomyopathy affect renal perfusion and autoregulation, additional mechanisms are at work as well. Visceral fat has been shown to be productive of angiotensinogen, therefore, angiotensinogen levels are elevated with rising BMI. This surplus of angiotensinogen leads to efferent arteriolar constriction, increased glomerular pressure, resultant cellular proliferation, and culminates in the development of glomerular injury.\textsuperscript{20,21}

\textbf{Endocrine}

Along with cardiovascular and pulmonary dysfunction, the interplay between obesity and the endocrine system, most notably in relation to type II diabetes and insulin resistance, has been well documented. It is well known that obesity is associated with elevated baseline insulin levels and hyperglycemia; however, it has also been shown when exposed to traditional stimulants of insulin secretion, the obese patient shows a heightened response.\textsuperscript{22} In addition, the hypothalamic-pituitary axis is hyperactive in obesity, particularly abdominal obesity with visceral adiposity, and it generates an environment characterized by increased levels of cortisol.\textsuperscript{23}

\textbf{Hepatic}

Hepatic abnormalities are also commonly seen in obese patients, and once again, a link is seen between dysfunction in this organ system and in others. Hyperlipidemia and lipotoxicity are each implicated in the development of nonalcoholic fatty liver disease and nonalcoholic steatohepatitis. This is promoted by insulin resistance-induced dysregulation of lipolysis in peripheral tissues, leading to intrahepatic accumulation of fatty acids.\textsuperscript{24,25}

\begin{figure}
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\caption{Anatomic and physiologic complications of obesity. Obesity is marked by the presence of widespread anatomic and physiologic changes. Many of these features are inter-related, leading to complex, multifactorial organ dysfunction.}
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Hematologic
As mentioned, the obese patient exists in a proinflammatory state, and as the adipose tissue mass increases, so does the risk for thrombotic events. The adipose tissue itself produces both tissue factor and plasminogen activation inhibitor-1, both of which promote thrombosis. Platelet function is a separate concern, with obese patients demonstrating evidence of platelets that are hyperactive and resistant to anticoagulant stimuli.

Musculoskeletal
Obesity is associated with a weight-associated increase in stress on bones and joints, so it is not surprising that obese patients are more likely than lean patients to report musculoskeletal pain, and to rate that pain as severe. Interestingly though, obese patients more commonly experience osteoarthritis of not only the load-bearing joints of the hips and knees, but also the shoulders, suggesting that factors other than simple overload are perhaps responsible. Regardless of the underlying etiology, loss of excess weight has been shown to reduce the musculoskeletal pain associated with obesity.

CHRONIC INFLAMMATION: THE COMMON THREAD IN OBESITY-RELATED ILLNESS
Obesity has been known for years to be a state of active and ongoing inflammation. In 1993, Gokhan Hotamisligil documented elevated concentrations of tumor necrosis factor (TNF-α) arising from the adipose tissue of obese patients and was able to link this marker of heightened inflammation with the development of insulin resistance. This sentinel discovery led to an explosion of investigation into inflammation in the obese patient, and the combined efforts have both enhanced our understanding of obesity and its related conditions and added complexity to the discussion of obesity-related illness.

Obese patients show a systemic proinflammatory state at baseline. C-reactive protein levels are higher in “healthy” obese patients, and they demonstrate leukocyte counts that are greater than those in normal BMI counterparts. In addition to the previously mentioned TNF-α, several cytokines have been associated with adiposity and obesity (Fig. 2). Interleukin (IL)-6 is the classic proinflammatory cytokine, and its levels are elevated in excess adiposity; the amount of IL-6 correlates with the amount of adipose tissue, and the adipose tissue

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Figure 2. Adipose tissue and inflammatory dysfunction. As adipose tissue increases due to a multitude of factors, changes are seen in cytokine and adipokine concentrations, largely because of adipose tissue production. These changes denote a shift to a proinflammatory environment characterized by changes in monocyte and macrophage populations as well as endothelial cell dysfunction. This heightened state of inflammation has been strongly linked to development of insulin resistance. ICAM, intracellular adhesion molecule; IL, interleukin; MCP, monocyte chemoattractant protein; MIP, macrophage inflammatory protein; TNF, tumor necrosis factor; VCAM, vascular cell adhesion molecule.
itself is implicated in IL-6 production. Interleukin-8, a neutrophil chemoattractant, is also produced by adipose tissue, and interestingly, stimulation of adipocytes with lipopolysaccharide leads to dramatic increases in IL-8 production. While these proinflammatory cytokines are produced in greater amounts, the classic anti-inflammatory cytokine, IL-10, is expressed in lower levels in the obese patient.

Aside from traditional markers of inflammation, adipose tissue is known to produce unique signaling agents known collectively as adipokines. The 2 best characterized of these are leptin and adiponectin. Leptin level correlates with BMI, and it appears to play a regulatory role in energy balance, with leptin receptor activation leading to decreased food intake and increased energy use. Leptin’s effects on the immune system include an upregulation of monocytes, a reduction in T-lymphocyte apoptosis, promoting an immune shift to TH1 phenotype, and enhancement of phagocytic activity. Adiponectin, on the other hand, is an adipokine that shows depressed levels in obesity and seems to have anti-inflammatory effects. Adiponectin reduces monocyte production of proinflammatory TNF-α and IL-6, and increases monocyte production of anti-inflammatory IL-10 and IL-1RA. In addition to leptin and adiponectin, omentin, apelin, resistin, visfatin, and adipsin all may have modulatory effects. This proinflammatory milieu of cytokines and adipokines in obese patients appears to be far reaching in its effects. Neutrophil function in obese patients is generally believed to be similar to that in patients of normal BMI; however, monocyte and macrophage function appears to be perturbed. Adipose tissue macrophages are present in greater numbers in the obese and they demonstrate a shift toward an M1 (proinflammatory) phenotype.

Macrophages distant from the adipose tissue are also involved in the pathophysiology of obesity, as more of these cells are seen in atherosclerotic plaques of obese patients when compared with normal BMI patients, and pulmonary alveolar macrophages appear to be activated in obese subjects whether or not obstructive sleep apnea is present. Long-term adaptation to infectious stimuli seems to be impaired as well, with obese subjects demonstrating decreased responsiveness at 1 year after influenza vaccination. The impairment appears to be secondary to reduced percentages of, and defective functioning of, CD8+ T-cells. Further, endothelial cell function is disrupted, with the general effect of obesity being induction of oxidative stress and upregulation of adhesion molecules, promoting both local and systemic inflammation.

**THE INJURED OBESE PATIENT**

As the numbers of obese have risen in the general population, their numbers have increased in the realms of critical care and trauma in kind. Depending on the specifics of the ICU studied, obesity prevalence ranges from 5% to 25%. When looking specifically at trauma patients, Christmas and colleagues noted that between 1993 and 2003, the proportion of trauma patients who were morbidly obese increased from 0.4% to 1.5%. Further, in a review of the Medical Expenditure Panel Study, Finkelstein and colleagues demonstrated that there is a direct correlation between increasing BMI and the risk of sustaining injuries, with morbidly obese patients having an annual risk of injury 48% greater than in those of normal BMI. This section will focus on the existing literature devoted to the care of the injured obese patient.

**Injury mechanisms and patterns in the obese patient**

Although obese individuals are subject to the same sources of traumatic injury as others, they are more prone to falls, and abnormal biomechanics appear to play a role in this propensity. Several authors have noted that the obese seem to share common patterns of injury, particularly after blunt trauma. Arbabi and colleagues reviewed a series of automobile collisions and found that obese patients tended to have lower injury severities overall, but had more severe extremity injuries than lean counterparts. This finding has been substantiated by others looking at all mechanisms of injury, and these authors found that in addition to extremity injuries, the obese patient has a proclivity to sustain thoracic trauma. The consensus appears to be that the obese patient sustains fewer traumatic brain injuries; however, Tagliaferri and associates actually found that more obese suffered severe traumatic brain injuries in an assessment of victims of front-end automobile collisions, and Brown and coworkers found that obese patients with traumatic brain injury fared worse, but they could not attribute this to obesity. In pediatric trauma patients, similar patterns have been seen, with the additional findings that obese youth sustain fewer intra-abdominal injuries and their brain injuries, on the whole, are less severe.

**Resuscitation and assessment of the obese trauma patient**

For a variety of reasons, the obese trauma patient may be difficult to evaluate and resuscitate. Theoretically, emergent intubation may be more difficult secondary to anatomic features, particularly in the setting of cervical spinal immobilization; however, in a study of emergent...
intubations at the New Jersey Trauma Center, Sifri and colleagues\textsuperscript{59} reported no difference in the rates of failed intubation or need for surgical airway in obese trauma patients, with the caveat that the majority of their intubations were performed by anesthesiologists. Even in the setting of a patent airway on initial assessment, it is critical to recognize that the obese trauma patient remains at increased risk for hypoventilation, particularly as spinal precautions with flat positioning are used and maintained and as narcotics are used for pain control. This may warrant the use of noninvasive positive pressure ventilation. Although this has been shown to be of value in the management of intermittent airway obstruction in obesity,\textsuperscript{60} it must be carefully used to avoid gastric distention and subsequent risk for aspiration events.\textsuperscript{61} Intravenous access is known to be more difficult to obtain and maintain in critically ill obese patient\textsuperscript{62}; however, this issue has not been assessed specifically in the setting of trauma. The Focused Assessment with Sonography in Trauma (FAST) examination has become a routine component of the evaluation of trauma patients in many centers, and many authors have indicated that the study has limitations in the obese;\textsuperscript{63,64} one important finding from the medical literature relevant to this issue is that echocardiography in the obese patient is known to carry the risk of a false positive finding of a pseudopericardial effusion.\textsuperscript{65} We have recently explored this issue, finding that a FAST examination performed by certified ultrasonographers followed by interpretation by an attending radiology staff showed a sensitivity of 85\% in patients of normal BMI, but only a 63\% sensitivity in the obese after blunt injury (Winfield and colleagues, manuscript in preparation).

Monitoring the response to resuscitation is difficult as well. Belzberg and colleagues\textsuperscript{66} evaluated pulmonary artery catheter measurements in a series of trauma patients admitted to the Los Angeles County Medical Center, finding that when compared with patients with BMI less than 30 kg/m\textsuperscript{2}, the 131 obese patients in their study showed elevated heart rates, decreased oxygen delivery, and decreased peripheral tissue oxygenation. Central venous pressures are commonly used as an indicator of adequacy of volume resuscitation, but this has known limitations, and its use may be completely unhelpful in the obese. We have demonstrated, in a large series of severely injured blunt trauma patients, that central venous pressure correlates well with BMI, but does not necessarily indicate appropriate resuscitation.\textsuperscript{67} To that point, in the same study, we assessed traditional metabolic parameters of resuscitation including pH, base deficit, and lactate, demonstrating that obese and morbidly obese patients showed a failure to resolve the pH and base deficit, but not lactic acid, despite receiving similar resuscitation to patients whose BMI was less than 30 kg/m\textsuperscript{2}. This was confirmed in a subsequent study by Nelson and colleagues,\textsuperscript{68} who studied 1,084 patients with an Injury Severity Score \( \geq 16 \) in Zurich, finding that obese patients received less fluid per BMI point, failed to resolve traditional metabolic parameters, and were more prone to hypovolemic shock, mortality, and organ failure than patients of normal BMI.

**Postinjury management and complications in the critically injured obese patient**

Elective and emergency surgery performed on the obese is known to be associated with poorer outcomes, and procedures performed after acute trauma are subject to greater complication rates as well. Duchesne and coauthors\textsuperscript{69} looked at 53 obese and morbidly obese patients requiring damage control laparotomy; they reported an increase in infectious and noninfectious complication rates and a greater incidence of failure to achieve primary fascial closure when compared with patients with BMI less than 30 kg/m\textsuperscript{2}. Similarly, when Haricharan and colleagues\textsuperscript{70} looked at this same issue, they found that obese patients required more than twice as many days on average (8.4 vs 3.9) to achieve fascial closure as their normal BMI counterparts. In obese patients with severe open book pelvic fractures, complication rates are higher because external fixation is subject to greater failure rates, and early symphyseal plating has been associated with improved outcomes.\textsuperscript{71} Additionally, Sems and colleagues\textsuperscript{72} found that obese patients with pelvic fractures were significantly more likely to undergo reoperation for failure of initial operative management. Repair of femur fractures has been shown to be subject to high complication rates, but there are some data suggesting that the use of retrograde, as opposed to anterograde, nailing techniques can decrease some of the morbidity secondary to decreased operative times and radiation exposure.\textsuperscript{73} With regard to ankle fractures, obesity does not appear to affect outcomes in the absence of comorbidities.\textsuperscript{74} Lower extremity vascular injuries can be more difficult to detect in the obese patient secondary to extremity girth and soft tissue. Simmons and colleagues\textsuperscript{75} showed similar outcomes in obese patients sustaining lower extremity vascular trauma, but in the morbidly obese subset of patients studied, there was a greater risk of progression to amputation and death in patients with these injuries.

Several authors have looked at the care needs and related challenges and complications in obese patients with prolonged critical illness. Winkelman and Maloney\textsuperscript{62} evaluated resource use in the ICU, finding that the obese
had a greater likelihood of special mattress use, more difficulty obtaining and maintaining intravenous access, and were more likely to require special equipment to deliver adequate care. Mobilization appears to be an issue for both the patient and nursing staff, and this combination of stasis, trauma, and pre-existing prothrombotic state likely at least partially explains the increased risk of deep venous thrombosis and decubitus ulcers seen in the series reported by Newell and coworkers. With regard to nutritional needs, calculations of resting energy expenditure using standard formulas are fraught with error, and indirect calorimetry appears to be a better means of ensuring nutritional needs in the obese. At present, the American Society of Parenteral and Enteral Nutrition (ASPEN) recommends that hypocaloric, high protein nutrition be provided to the critically ill obese patient, based on the finding that this maintains an equivalent nitrogen balance; however, this recommendation is only grade D, as studies are limited and have not been correlated with improved outcomes. Several authors have demonstrated an increased number of ventilator days in the obese patient, and this may necessitate tracheostomy. Aldawood and associates found a greater major complication rate (12% vs 2%) in obese patients undergoing percutaneous tracheostomy, while El Solh and Jaafar demonstrated greater overall complication rates (25% vs 14%) in the setting of open tracheostomy in morbidly obese patients.

There is some support in the literature for the concept that injured and critically ill obese are subject to greater rates of hospital-acquired infections. Bochicchio and colleagues prospectively looked at a cohort of 62 obese patients, finding them to be twice as likely to develop bloodstream, urinary tract, or pulmonary infections as compared with lean patients. This was confirmed in a group of morbidly obese patients in the large retrospective series by Newell and colleagues, with overall increases in these infections seen with increases in BMI classes. We, along with Serrano and associates, found that overall infectious complications were greater as BMI class increased, although we noted a statistically significant difference only in urinary tract infections, while Serrano and coworkers’ series noted differences in wound and pulmonary infections. Dossett and coauthors looked specifically at bloodstream infections and catheter-related bloodstream infections in obese surgical ICU patients, finding an increased risk in the morbidly obese; they speculated that this was due to difficulty in obtaining intravenous access and a reluctance to discontinue intravenous catheters in this patient group, but did not collect data on the number of catheter days to support this assertion. Finally, Belzberg and colleagues and Brown and associates incidentally noted increases in the development of sepsis in injured obese adults and children, respectively.

There have been studies that indicate that obesity is perhaps not associated with increased infectious risk. Dossett and coauthors evaluated critically injured adults requiring ICU care for greater than 48 hours, including 286 obese and 81 morbidly obese patients; no difference in the rates of pneumonia between these groups and underweight, normal, or overweight patients was seen. Collier and collaborators reviewed CT scans on 281 obese patients and calculated body fat distribution as a ratio of visceral to subcutaneous fat based on the concept that visceral adiposity is more directly associated with the proinflammatory state of obesity; they found no difference in infectious complications in 140 patients with a visceral adipose distribution as opposed to 141 with a subcutaneous distribution.

The trauma literature has consistently shown an increased risk of organ failure and multiple organ failure (MOF) in obese patients. Neville and associates compared 63 obese with 179 nonobese patients, finding a significantly greater rate of MOF in the obese (13% vs 3%); however, the series did not report the objective criteria used to make this determination. Using the Denver scoring system, Ciesla and associates reviewed 716 severely injured patients, and in a multivariate analysis, found that obese patients showed a higher rate of MOF, and specifically identified differences in the rates of ARDS, cardiac, and hepatic failure. In their series evaluating hemodynamic parameters, Belzberg and coauthors demonstrated increased ARDS and renal failure; however, this was not adjusted for age or comorbidities. In the largest retrospective series in the current literature, Newell and colleagues divided 1,543 patients according to NIH BMI classification; using the National Trauma Registry of the American College of Surgeons criteria to define organ failure, they showed stepwise increases in the risk of MOF as BMI class increased, with significantly greater risks of MOF, ARDS, renal failure, and acute respiratory failure in the morbidly obese patient group as well as a greater risk of acute respiratory failure in obese patients. We controlled for traditional predictive factors as well as blood transfusions, demonstrated correlation between BMI class and MOF development using the Marshall scoring system in 455 severely injured blunt trauma patients, and found that renal failure scores increased with increasing BMI. Finally, Duchesne and coworkers found that among patients undergoing damage control laparotomy, obese and morbidly obese patients were more likely to develop MOF, specifically...
finding an increased risk of acute renal failure, based on an increase in creatinine of 50% over baseline.

Outcomes in the injured obese patient

Many of the existing articles in the trauma literature use traditional measures such as length of stay (LOS), ICU LOS, ventilator days, and mortality as outcomes descriptors (Table 1). Choban and colleagues provided the initial report of worsened outcomes in obese trauma patients, indicating that the obese showed no difference in LOS or ventilator days, but worsened mortality rates after controlling for age and Injury Severity Score. The report’s current applicability is limited by the use of nonstandard BMI grouping, with the obese group being referred to as “severely overweight,” with BMI > 31 kg/m²; however, the authors were the first to recognize and document the measurable impact that obesity was having on the care of trauma patients and set the table for future explorations into the subject. The balance of the literature does suggest that obese trauma patients have longer LOS, longer ICU LOS, and more ventilator days, although not all series demonstrate these findings.

One of the more interesting aspects uncovered during review of the trauma literature evaluating outcomes is that although the majority of reports indicate greater complication rates in obese patients, including MOF, there is no clear association with mortality. This has led some to question as to whether obesity has an overall protective effect against mortality after severe injury, representing a so-called “obesity paradox.” Finally, some authors have suggested that obesity itself is not associated with poorer outcomes in the critically injured; instead, they hypothesize that insulin resistance and diabetes, independent of obesity or morbid obesity, are in fact stronger predictors of mortality. Diaz and associates evaluated 1,134 patients with a mean Injury Severity Score of 25.7 at the Vanderbilt University medical center, dividing them on the basis of either BMI or admission hyperglycemia (mean glucose > 150 mg/dL in the initial 24 hours of hospitalization). Although morbid obesity was not associated with an increased mortality in their series, hyperglycemia was an independent predictor. The study is limited overall by the comparison of morbidly obese patients with all others, including the

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LOS, length of stay.
immune dysfunction in the obese trauma patient
Given the extensive amount of literature devoted to the inter-related nature of obesity and inflammation and the frequent findings of postinjury organ failure and infectious complications in the obese trauma patient, several authors have theorized that altered immune responses may play a role in the poorer outcomes seen; however, this concept has only been preliminarily explored. We were the first to evaluate this possibility in human subjects through evaluation of the genomic samples collected as a part of the “Inflammation and the Host Response to Injury” project. Looking at the whole-genome expression in a mixed leukocyte population among 163 severely injured trauma patients, comparing these signatures on the basis of BMI classifications within 12 hours of injury, we found that there were no significant differences between BMI groups at that time point, suggesting that there was no difference in the early immune responses of these groups. We did evaluate serial samples from these patients out to 28 days postinjury, finding divergence in genomic expression over this time course across BMI groups. Limitations included the use of a mixed leukocyte population, which would be predominantly polymorphonuclear cells early in the postinjury response, but which would shift over time; furthermore, determination of whether differential genomic expression over time was the cause of (or the response to) complications in the obese was impossible due to the retrospective nature of the study. We followed this with an analysis of serum cytokines in obese and patients of normal BMI from the same dataset, focusing on the first 4 days after injury. In contrast to our evaluation of the leukocyte genome, we found dramatic differences in cytokine concentrations, demonstrating depressed serum cytokine levels in the obese relative to lean counterparts with similar injury severity. This suggested a surprising state of early immune suppression. Based on this, we hypothesized that early immune suppression may contribute to later infections and organ failure in the obese. The sole remaining study of postinjury immune dysfunction in obese trauma patients was performed by Collier and colleagues, who examined differences in serum cytokine levels between obese patients with visceral adiposity and those with subcutaneous adiposity, finding no difference in cytokine levels between the 2 patient groups.

THE INJURED OBESE PATIENT: A LOOK AHEAD
Based on current trends, it is safe to say that obesity will continue to challenge trauma care providers in the coming years. In order to face this challenge, accumulation of new data and development of novel techniques geared toward the care of the obese patient will be necessary. In the next section, additional findings on the topic from the basic science and medical literature will be explored, and areas of potential future investigation will be highlighted.

Considerations in the care of the injured obese patient
In some respects, initial assessment of the obese trauma patient is no different than that of any patient presenting for evaluation of injuries. That said, providers can anticipate certain issues, and may need to adapt their personal or institutional approach when the obese present for care after significant injury.

We earlier reviewed data suggesting that airway management, or at least emergent endotracheal intubation, does not appear to be any riskier in the obese trauma patient; however, this is not definitive, and given the known anatomic challenges and lack of pulmonary reserve in this population, we feel strongly that the obese patient warrants the attention of experienced care providers familiar with advanced airway techniques. With regard to initial circulatory management, data from the ICU support the concept that obtaining and maintaining intravenous access may be challenging. The optimal methods for obtaining emergent intravenous access in the obese have not yet been systematically determined; nonetheless, given the known anatomic perturbations present, we would once again advocate early involvement of practitioners comfortable with a variety of access techniques to facilitate this critical step. As patients are resuscitated, it is important to remember that cardiac and vascular dysfunction is common in the obese, standard physiologic parameters as well as noninvasive and invasive means of measurement are likely to be inaccurate, and traditional endpoints of resuscitation are limited in their efficacy. This is an area desperately requiring further investigation, both in terms of developing novel resuscitative algorithms, and in determining more appropriate endpoints. In our study evaluating traditional endpoints of resuscitation, one issue that we were unable to completely explore was whether volume resuscitation should be based on actual or ideal body weight; because one possible explanation for the failure to resolve measures such as base deficit and pH is volume under-resuscitation, this may have...
important implications for therapy. Our database did not include detailed data on the resuscitation fluids used or on electrolyte concentrations, the implication being that patients may have been over-resuscitated with normal saline, leading to development of a hyperchloremic metabolic acidosis. The final possibility is that of a metabolic explanation for the perturbations seen, and this would clearly be possible in the setting of known alterations in insulin concentrations and altered glucose metabolism. All are possible and represent areas of potential study.

Consideration of appropriate monitoring techniques should also be contemplated. In moderate to severely injured obese patients, it may be reasonable to more aggressively use pulmonary artery catheters and transesophageal echocardiography to guide resuscitation given the inadequacy of less invasive measures and the technical challenge of transthoracic echocardiography in the obese; however, the risks of these more invasive techniques should be weighed against perceived benefits. Using central venous oxygen saturation measurements and so-called minimally invasive hemodynamic monitoring devices (eg, Vigileo and FloTrac, both Edwards Lifesciences) may prove useful as well, but their use has not been specifically studied in the obese and requires further investigation. Finally, the impact of resuscitation on organ failure calls for additional study. Sugerman demonstrated that truncal obesity leads to chronically elevated intra-abdominal pressure, which contributes to physiologic change and organ dysfunction. Even with relatively modest volume resuscitation, the obese patient is at greater risk for development of intra-abdominal hypertension, so in trauma, where volume resuscitation may be significant, the obese patient may be at heightened risk for abdominal compartment syndrome and its sequelae, to include multiple organ failure.

In regard to longer-term management, several issues should be considered. Nutrition seems to be of significant importance, given its inter-relationships with pulmonary function, endocrine homeostasis, and immune/inflammatory function. As previously highlighted, existing reports recommend the use of high-protein, hypocaloric feeding regimens in the obese; however, these data are limited to small series and largely focus on the outcome of achieving positive nitrogen balance and generally have not studied clinical benefit. In addition to gross compositions of support formulations, other components that have received some attention are the use of immune-modulating agents such as L-arginine, fish oil, and vitamin E. In general, these show promising theoretical anti-inflammatory benefits, but lack rigorous study demonstrating clinical advantage. An additional and intriguing possibility is that of bacterial flora manipulation. Studies have demonstrated differences in gut microbiota when comparing obese with lean patients, and this is theorized to contribute to obesity and a diminution of gut barrier function; therefore, manipulation of the microbiota by prebiotics or probiotics may have dual beneficial effects in obese patients. Although not rigorously studied to date, providing therapeutic immunonutrition may prove to be of substantial benefit to the obese trauma patient.

The obese trauma patient is at a significantly increased risk for venous thromboembolic (VTE) phenomena due to the pre-existing hypercoagulable state of obesity, the additional inflammatory stimuli resultant from trauma, and the environment of stasis created by difficulty in turning and mobilization due to patient habitus and the issue of acute or chronic pain. As such, an area that mandates additional attention is in prophylaxis for VTE. The most recent guidelines of the American College of Chest Physicians acknowledge that trauma patients are at increased risk for VTE and that obese patients undergoing elective surgery are at increased risk for VTE; however, clear guidelines for the management of this patient group are lacking. Studies from the bariatric surgery literature support the use of higher dosing of low-molecular weight heparin, but a uniform regimen has not yet been established; based on newer studies in the trauma literature, this will likely be optimized based on anti-Xa measurements or thromboelastography, rather than a pure weight-based adjustment. Injury screening protocols may also require a different approach in the obese patient. The use of ultrasound appears to be unreliable, as was indicated previously. Based on our findings, we recommend foregoing the FAST examination and performing CT scan to evaluate hemodynamically stable obese patients for blunt intra-abdominal injury.

Areas for scientific investigation in obesity and trauma

Just as clinical care stands to be improved; further work should be done to elucidate the mechanisms and consequences of immune dysfunction in the injured obese patient. This has begun in retrospective human studies, but more information is likely to be gained through prospective human and animal studies. Among the first steps will be to characterize the nature of the immune function and dysfunction that is occurring. Matheson and colleagues at the University of Louisville, speculated that the liver is a source of immune hyperactivity in the traumatized obese. Using a model of hemorrhagic shock in Zucker rats that focuses on the effects of hepatic ischemia-reperfusion, they have demonstrated that relative to lean littermates, obese rats are more susceptible to hepatic ischemia and reperfusion, and that this leads to an elevated inflammatory response at 4 hours noted
by increased IL-6, IL-1B, and HMGB1 (high-mobility group box 1) concentrations. They indicate in their study that there is remote organ damage based on elevated blood urea nitrogen in obese rats subjected to shock relative to lean littermates and obese rats not subjected to this insult; however, there are no significant differences seen in creatinine concentrations between obese rats subjected to and not subjected to shock. In contrast to this proinflammatory scenario, our human data suggest that there is a state of early immune suppression based on low systemic cytokine concentrations in the first hours and days after injury, and we have considered the possibility that this is reflective of a state of tolerance due to a chronically active immune system at baseline. This is supported by our finding that later multiple organ failure occurs in these patients, possibly due to greater numbers of infectious complications. There is some precedent in the basic science literature for this finding of greater susceptibility of the obese subject to particular types of infections, with diet-fed obese mice showing increased susceptibility to both Porphyromonas gingivalis and Staphylococcus aureus infections relative to lean animals due to dysfunctional macrophage activity.103,104

One component of the immune response that has not been probed extensively in trauma is that of adipokine concentration and kinetics. This would seem to be worthy of study, given the direct relationship of these substances with excess levels of adipose tissue. From the medical literature, low levels of leptin appear to denote poorer outcomes in the critically ill. Bornstein and associates105 showed that in contrast to healthy controls, critically ill patients showed a lack of diurnal variation in leptin concentration; in a study of medical ICU patients, Koch and coauthors106 found that lower leptin levels were associated with increased mortality. In contrast, low adiponectin concentrations seem to be beneficial in critical illness. In a separate study, Koch and coworkers107 showed that low adiponectin concentrations were seen in obese patients on admission to the ICU and that this was associated with improved survival. In their animal studies, Matheson and colleagues101 demonstrated elevated levels of both leptin and adiponectin in obese rats; however, because these are counter-regulatory adipokines, the potential clinical significance of this is unclear. Ghrelin is the only other adipokine studied in trauma or critical illness to date; Kwan and coauthors108 linked ghrelin to a decrease in microvascular permeability in the rat mesentery in an in vitro model. They speculated that because obese patients have lower baseline levels of ghrelin, poorer outcomes in obese patients may be secondary

Figure 3. Schematic of obesity-related dysfunction after major trauma. Obesity is a state of chronic inflammation complicated by metabolic and physiologic derangement and anatomic variance. In the setting of severe injury, these baseline alterations contribute in a multifactorial fashion to create an environment in which the obese patient is at greater risk for postinjury complications due to internal dysfunction compounded by challenges faced by health care staff in delivering best-practice care.
to a worsened inflammatory response characterized by greater microvascular leak.

CONCLUSIONS
In summary, obesity is a worldwide problem that is growing in scope. In addition to their size and associated anatomic variances, obese patients have underlying physiologic and biochemical perturbations that make them difficult to care for; these same features add complexity to their care after major injury and contribute to poorer outcomes. We have proposed a multidimensional model outlining features of obesity that contribute to poorer outcomes (Fig. 3). Within this model, there are tasks facing the trauma provider from the cellular level to clinical practice, and as trauma care providers are faced with increasing numbers of obese patients, fully defining the physiologic and immune responses to injury and using these data to develop tailored care protocols for the obese represent the only opportunity to produce optimal outcomes in this challenging patient population.

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REFERENCES


