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Invited Review

Perioperative management of the obese surgical patient

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Abstract

Introduction: The escalation in the prevalence of obesity throughout the world has led to an upsurge in the number of obese surgical patients to whom perioperative care needs to be delivered.

Sources of data: After determining the scope of the review, the authors used PubMed with select phrases encompassing the words in the scope. Both preclinical and clinical reports were considered.

Areas of agreement: There were no controversies regarding preoperative management and the intraoperative care of the obese surgical patient.

Areas of controversy: Is there a healthy obese state that gives rise to the obesity paradox regarding postoperative complications?

Growing points: This review considers how to prepare for and manage the obese surgical patient through the entire spectrum, from preoperative assessment to possible postoperative intensive care.

Areas timely for developing research: What results in an obese patient developing ‘unhealthy’ obesity?

Key words: obesity, surgery, intensive care
Introduction

Over the 150-year period between 1850 and 2000, life expectancy in the US more than doubled; however, with the start of obesity epidemic, beginning in the late 1970s, the rate of increase in life expectancy has plateaued and in 2015 it began to decline. This decline is due to a significant increase in deaths related to the obesity complications of cardiac disease, diabetes, chronic liver disease, and stroke. These, as well as other obesity-related diseases, such as musculoskeletal disorders, and several cancers (endometrial, breast, ovarian, prostate, liver, gall bladder, kidney and colon) frequently require surgical interventions and therefore the need for perioperative and critical care of the obese surgical patient is set to increase remarkably. These concerning demographic trends are likely to be replicated throughout the developed world and provide a good reason for a topical review on the clinical management of the obese surgical patient.

Though obesity is associated with greater morbidity than smoking, alcoholism and poverty and will overtake cigarette smoking as the leading cause of preventable deaths, there exists an ‘obesity paradox’ in which obesity is somehow protective against mortality that was reported in retrospective analyses of several chronic wasting diseases. The obesity paradox was first identified in the setting of systolic heart failure and has now been found in chronic renal failure, chronic obstructive pulmonary disease and cancer. Recently, the obesity paradox has been challenged as an artifact arising from the ‘single snapshot’ body mass index (BMI) measurement that does not longitudinally represent the subject’s long-term adiposity when contemporaneously measured. However, when obesity-induced diabetes supervenes the paradoxical survival benefit is eliminated. Furthermore a recent study involving more than 0.5 million subjects reported that even in the absence of metabolic derangements, obese patients are more likely to develop cardiovascular complications.

Definition and diagnostic criteria

Obesity can be established according to either anthropometric or body composition diagnostic criteria.

The BMI, defined as weight in kilograms divided by the height in meters, squared, provides a value in units of kg/m², although these units are often omitted. According to the NIH, overweight encompasses subjects between 25.0 and 29.9 while Obesity (I) is defined as 30.0–34.9 and Obesity (II) as 35–39.9. Patients with a BMI ≥ 40 are referred to as having extreme or morbid obesity (III) (Table 1). The weakness of the BMI is that it cannot discriminate between adipose and non-adipose tissue in the individual although it does correlate with total body adiposity at the population level. There can be no universal threshold BMI values for the diagnoses of overweight/obesity.

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morbid obesity. Using Caucasians as the standard, African-Americans have a 1.3 kg/m² higher BMI and Indonesian and Thai people have a 3 kg/m² lower BMI at the same level of body fat.\textsuperscript{19} In Caucasian populations, obesity is defined as a body fat compartment of 25% in adult males and 35% for adult females. Densitometry, using water displacement, underwater weighing or air displacement, is a laboratory-based technique for deducing the fat mass (0.9 kg/L) from the fat-free mass (1.1 kg/L) based upon the differences in density in these two compartments. Dual energy X-ray absorptiometry (DXA) scans can distinguish mineral from soft tissue, and within soft tissue, of lean mass from fat mass based upon their different energy attenuation coefficients. Other scanning techniques including computed tomography (CT) and magnetic resonance imaging (MRI) identify adipose tissue directly and then assume that 80% of adipose tissues is made up of fat. Because of the radiation and costs of whole body scans, these techniques are usually only employed for assessment of the distribution of fat. Outside the laboratory setting, skinfold thickness, usually from four different sites (biceps, triceps, subscapular and supra-iliac), are used for estimating total body fat because the relationship between subcutaneous fat and total fat is relatively constant. Bioelectrical impedance may also be used for assessing total body fat.

**Prevalence**

In the United States, the National Health and Nutritional Examination Survey (NHANES) reports annually on the prevalence of obesity using the BMI. Between 1960 and 1980 the overall prevalence of obesity (BMI $\geq$ 30) was fairly constant at approximately 14% for men and women aged 20–74 years.\textsuperscript{20} By 1994, the prevalence of obesity had increased to 21%. In the most recent analysis of NHANES data for 2014, the prevalence of age-adjusted obesity amongst US women was 40.4%, which represents a significant increase from the data surveyed a decade earlier when controlled for age, race, smoking status, and educational attainment.\textsuperscript{21} For men the prevalence was 35% with no significant trend from the prior decade. The prevalence of morbid obesity (BMI $\geq 40$), had reached 10% in women by 2014, again a significant increase from the previous decade, while in men it was relatively constant at 5.5%.\textsuperscript{21}

In 2- to 19-year-olds in the US, the prevalence of obesity was 17.0% and morbid obesity was 5.8%.\textsuperscript{22} Regarding trends, the rates have decreased in children aged 2–5 years since 2003–04, stabilized in 6- to 11-year-olds since 2007–08, but steadily increased among adolescents since 1988.\textsuperscript{23} In the EU, approximately 40–50% of men and 25–35% of women are overweight and 15–25% of men and women are obese.\textsuperscript{24} According to the WHO, 41 million children >5 years had a BMI $> 25$%.\textsuperscript{25} Worldwide, the prevalence of obesity in adults will reach 18% in men and surpass 21% in women; severe obesity will surpass 6% in men and 9% in women.\textsuperscript{26}

**Causes of obesity**

Weight gain can be explained as an energy imbalance between calories consumed and calories expended. A coordinated network of central mechanisms, that include the hypothalamic arcuate nucleus, and peripheral signals, including from the microbiome and cells within adipose tissue, stomach, and pancreas, control short-term and long-term energy balance.\textsuperscript{27} Emphasis on exercise, better dietary choices and nutritional content labeling of foods have been advocated as methods for reversing the energy imbalance.\textsuperscript{22} Yet, these strategies have not resulted in a reversal of the trend in the obesity epidemic possibly because of lack of compliance or because of the advent of counter-regulatory central orexigenic signals that increase appetite and food intake thereby limiting the degree of predicted weight loss that is associated with interventions such as exercise programs.\textsuperscript{28} Alternately, some have advocated that reliance exclusively on only diet (energy intake) and exercise (energy expenditure) ignores many other factors including the contributing role of sleep disturbance.\textsuperscript{29} Occupational factors may also contribute to the obesity epidemic as the daily occupation-related
energy expenditure has declined by >100 calories over the past 50 years. Environmental influences for weight gain are evidenced by the inverse relationship between obesity and socioeconomic class as well as the trend toward increasing obesity in developing countries associated with urbanization. Furthermore, there has been a displacement of leisure-time physical activities with sedentary activities dominated by the use of electronic devices. Another factor is thought to be the plethora of drugs that have, as a side-effect, weight gain.

Genetics may also be a possible cause for the dysregulation between caloric intake and expenditure. A combination of family, twin and adoption studies have demonstrated that the heritability of BMI is between 0.71 and 0.86 although the specific genes have not been identified. An overarching concept of genetic influence suggests that the easy availability of food has rendered superfluous ‘thrifty genes’, that favor survival during periods of famine; this theory has been challenged. There are 11 rare monogenic obesity diseases that are caused by mutations in the leptin/melanocortin-4 receptor pathways that can produce severe obesity especially in children. Recently, epigenetic factors have also been mooted as a cause of the energy imbalance that results in obesity.

Sequelae of obesity

Obstructive sleep apnea (OSA) is characterized by repetitive partial or complete airway collapse during sleep causing hypoxemia and/or hypercarbia. Standard diagnosis usually requires overnight polysomnography and is defined as cessation of airflow of greater than 10 s with continued ventilatory effort, five or more times per hour of sleep, with a decrease in arterial oxygen saturation. Associated symptoms include snoring, daytime somnolence, sleep disruption, altered cardiovascular function, systemic and pulmonary hypertension, cardiac arrhythmias, myocardial ischemia, ventricular hypertrophy and failure. The prevalence of OSA is approximately 20% in the general population. Based on two large population-based studies, the Sleep Heart Health Study and the Wisconsin Sleep Cohort, up to 80% of individuals with less severe forms of OSA are undiagnosed while severe OSA is undiagnosed in approximately 10–20% of patients with BMI > 35. Undiagnosed and hence unsuspected OSA may lead to perioperative complications including difficult mask ventilation and/or intubation, postoperative reintubation, cardiac dysrhythmias and increased hospital length of stay.

Among the risk factors for the development of OSA, obesity has the most influence especially in those <50 years and this is bidirectional (Fig. 1). Studies on the relationship between weight change and progression and regression of OSA have found a strong correlation.

The treatment of choice for OSA is the use of devices that can maintain continuous positive airway pressure (CPAP) to ensure airway patency. Ill-fitting masks and discomfort from the devices cause a significant degree of non-adherence, defined by the CMS as use the CPAP device for <4 h per night for <70% of the nights in a consecutive 30-day period. In the search for higher patient compliance advances in design have resulted in newer masks such as the Bilevel positive airway pressure (BiPAP) devices which allow for distinct inspiratory and expiratory pressure settings.

Metabolic syndrome

A variety of criteria have been used to define the metabolic syndrome in the literature. The influential National Cholesterol Education Program (NCEP) defines metabolic syndrome as occurring when three or more of the following are present: (i) abdominal obesity (waist circumference, >102 cm in men or >88 cm in women); (ii) glucose intolerance (fasting glucose level, ≥100 mg/dL); (iii) hypertension, ≥130 mm Hg systolic and/or ≥85 mm Hg diastolic; and (iv) hypertriglyceridemia, ≥150 mg/dL or high-density lipoprotein cholesterol <40 mg/dL in men or <50 mg/dL in women.

In 2009, several major organizations, including the International Diabetes Federation and the American
Heart Association (AHA), required at least three of five criteria with hypertriglyceridemia now split into two separate elements and with the waist circumference cutoff being defined not only by sex but by ethnicity, and region (Table 2).  

The prevalence of metabolic syndrome in US adults using a revised AHA/NCEP definition has increased from 28% in the period between 1988 and 1994 to 34% in the period between 1999 and 2006.  

Using NCEP criteria the prevalence of metabolic syndrome in bariatric surgical patients was 80%.  

While several studies had shown that obesity is not associated in increased perioperative complications, morbidity or mortality (‘Obesity Paradox’), obese non-cardiac surgical patients with ‘modified’ metabolic syndrome (presence of hypertension and diabetes) were at increased risk for mortality, cardiac adverse events, pulmonary complications, acute kidney injury, stroke, wound complications and postoperative sepsis.  

Using the data from the National Inpatient Sample from the Hospital Cost and Utilization Project, posterior lumbar spine fusion patients with metabolic syndrome (presence of three out of the four conditions: obesity, hypertension, diabetes mellitus and dyslipidemia) had significantly increased rates of length of hospital stay and cardiac complications compared to patients without metabolic syndrome.  

Using the National Surgical Quality Improvement Program (NSQIP) database, hepatic resection patients with metabolic syndrome (BMI ≥ 30 kg/m² in the setting of concomitant diabetes and hypertension) had a greater risk for reintubation, >48 h of ventilator dependence, myocardial infarction and superficial surgical-site infections compared with patients without metabolic syndrome.  

As both acute illness and the perioperative period are associated with insulin resistance, surgical patients with metabolic syndrome are likely to develop hyperglycemia which increases the risk for postoperative
Thus far, there is little consensus regarding the blood glucose threshold for initiating therapy, the targeted blood glucose level, which therapies to use and for how long these should be maintained. Preoperative interventions

The importance of a preoperative assessment and management of the obese surgical patient population is highlighted by the associated increased risk of morbidity and mortality secondary to associated comorbidities including hypertension, diabetes, dyslipidemia and cardiovascular disease.

Obstructive sleep apnea

The Snoring, Tiredness, Observed apnea, high blood Pressure (STOP)-Body mass index, Age, Neck Circumference and Gender (Bang) screening tool has been extensively validated in surgical patients. In the obese, a STOP-BANG score >3 has a sensitivity of >90% for detecting OSA with a positive predictive value of 85%. A score of >5 has the sensitivity of 53%, specificity of 70% of predicting moderate to severe OSA.

There is a correlation between OSA severity and each of advanced age, cardiovascular disease and left ventricular dysfunction. The American Society of Anesthesiologists Task Force on Perioperative Management of Patient with OSA recommend that patients with confirmed or suspected OSA undergo preoperative assessment prior to the day of surgery with sufficient time to allow preparation and execution of a perioperative management plan. The preoperative assessment should include a comprehensive review of medical records including sleep studies, patient interview and physical exam. A focused interview in the setting of suspected OSA may include questions on snoring, apneic episodes, frequent arousals during sleep, morning headaches and daytime somnolence. The physical exam should include the airway, nasopharyngeal anatomy, neck circumference and tongue volume.

As the diagnosis of OSA is associated with a significantly increased incidence of postoperative complications including respiratory failure, postoperative cardiac events and unplanned intensive care admission, the preoperative preparation for patients with complications including surgical-site infection.

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<td>Population- and country-specific definitions</td>
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<tr>
<td>Elevated triglycerides (drug treatment for elevated triglycerides is an alternate indicator†)</td>
<td>≥150 mg/dL (1.7 mmol/L)</td>
</tr>
<tr>
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HDL-C indicates high-density lipoprotein cholesterol.

*It is recommended that the IDF cut points be used for non-Europeans and either the IDF or AHA/NHLBI cut points used for people of European origin until more data are available.

†The most commonly used drugs for elevated triglycerides and reduced HDL-C are fibrates and nicotinic acid. A patient taking 1 of these drugs can be presumed to have high triglycerides and low HDL-C. High-dose ω-3 fatty acids presumes high triglycerides.

‡Most patients with Type 2 diabetes mellitus will have the metabolic syndrome by the proposed criteria.


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### Table 2 Criteria for clinical diagnosis of the metabolic syndrome

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confirmed OSA may include CPAP or BiPAP, preoperative oral appliances\textsuperscript{70} and preoperative weight loss. Preoperative initiation and perioperative use of CPAP or BiPAP can reduce postoperative complications such as hypercarbia, hypoxemia and pulmonary artery vasoconstriction.\textsuperscript{71,72} Preoperative initiation of CPAP is recommended particularly if OSA is severe. There is insufficient evidence to support canceling or delaying surgery to perform sleep studies for definitive OSA diagnosis.\textsuperscript{73}

OSA is associated with increased sensitivity to central and peripheral effects of opioids\textsuperscript{74,75} including the respiratory depressant effects of opioids.\textsuperscript{76} Sleep disruption and nocturnal intermittent hypoxemia may enhance pain by acting directly or by activating inflammatory pathways.\textsuperscript{77,78}

### Cardiovascular disease

Obesity produces changes in cardiac morphology and ventricular function as an adaptation to excess body mass and increased metabolic demands.\textsuperscript{79} The excess body mass leads to an increase in cardiac output which progresses over time from left ventricular (LV) hypertrophy, to dilation, and ultimately to LV failure. Risk factors for coronary artery disease in the obese patient include diabetes, hypertension, dyslipidemia, inflammation, and a hypercoagulable state. A complete preoperative cardiac assessment should be obtained including a history and physical examination, and functional capacity. A patient’s functional status can be inferred from their ability to perform activities of daily living and higher cardiorespiratory fitness (established by metabolic equivalents [METS]) is associated with a lower risk of adverse cardiac events.\textsuperscript{80} However, the assessment of functional status can be difficult due to limited mobility in obese patients. A cardiac risk assessment should be performed using the American Heart Association (AHA) guidelines.\textsuperscript{81} According to the 2004 AHA guidelines, for patients who have elevated cardiac risk and poor or unknown functional capacity, exercise testing and/or cardiac imaging are reasonable management options.

In the obese population, barriers to testing may result from body habitus and weight limitations of diagnostic equipment. Overall, the need for further cardiac testing depends on consideration of the patient’s risk factors, cardiac risk determined by the planned surgery and the patients functional status. The American College of Surgeons NSQIP Risk Calculator and the Revised Cardiac Risk Index are validated tools for estimating perioperative risk.\textsuperscript{82}

Several population-based studies have demonstrated a direct relationship between obesity and hypertension.\textsuperscript{83} Some evidence exists to suggest that the use of angiotensin-converting-enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) may be beneficial secondary to their ability to increase insulin sensitivity.\textsuperscript{84} Obese patients have multiple risk factors for developing pulmonary hypertension, LV dysfunction, and pulmonary thromboembolism. Preoperative assessment for patients with pulmonary hypertension should include ECG and an echocardiogram to assess ventricular and valvular structure and function. Preoperative management should be conducted in conjunction with pulmonary and/or cardiology specialists to optimize the patient’s cardiopulmonary disease. The obesity surgery mortality risk score (OR-MRS) is a validated tool to stratify risk in the bariatric population. This tool uses five preoperative variable, including BMI, male gender, hypertension, known risk factors for pulmonary embolism, and age $\geq$45 years, to classify groups into low, intermediate, and high risk.\textsuperscript{85}

### Pharmacologic considerations of the obese surgical patient

While anesthetic drug-dosing is typically based on patient weight and clinical condition, in obesity the pharmacokinetic parameters of medications are altered. In obese patients, the amount of adipose tissue increases in proportion to the increase in total body weight, while the amount of lean body weight remains relatively constant resulting in a reduced proportion of lean body weight per kilogram. Consequently, the volume of distribution for lipophilic drugs is increased in obesity (Table 3).\textsuperscript{86} Changes in total blood volume and cardiac output also occur in obesity and can also affect pharmacokinetic parameters.\textsuperscript{87} Regional blood
flow must also be taken into account in obese patients as cardiac output remains directed at lean muscle and visceral organs. Thus, dosing hydrophilic drugs by total body weight instead of a measurement directed at lean body mass (LBM). The James formula is perhaps the most widely used for calculating LBM in the perioperative period and its practical use for target-controlled infusion in obese patients is well-explained by Absalom and colleagues.88

In addition to changes in pharmacokinetics, obese patients may have comorbid conditions that also determine the ultimate clinical effect of medication administration. For example, changes in plasma protein binding and hepatic metabolism due to obesity-induced hepatic steatosis may alter drug clearance.89,90 Patients with OSA, a frequent accompaniment of obesity (see above), have pharmacodynamic alterations with an increased sensitivity to certain sedatives.91

**Individual drugs**

**Benzodiazepines**

As these lipophilic medications have an increased volume of distribution (Vd) in obese patients,92 dosing should be determined by total body weight (TBW).

**Opioids**

In the distribution and clearance models used, the appropriate remifentanil infusion rate is governed by either ideal or lean body weight as dosing by total body weight may result in opioid overdose.93 Similarly, fentanyl dosing by total body weight also results in overdose; thus fentanyl should be dosed by IBW or LBW.94

**Propofol**

This lipophilic sedative-hypnotic is commonly used for the induction and maintenance of general anesthesia, propofol dosing by a total body weight has been found to be appropriate, without evidence of increased drug accumulation in obese patients.97

**Dexmedetomidine**

This alpha-2 agonist is used for sedation, anxiolysis and pain relief. When used intraoperatively as an adjunct with general anesthesia for bariatric surgery, its use resulted in opioid reduction, reduced recovery stay, reduced antiemetic dose.98 One study examined the influence of obesity on dexmedetomidine pharmacokinetics, and found that dosing dexmedetomidine based on TBW resulted in increased serum concentrations. This was due to volume of distribution increases dependent on lean body tissue, and a reduced clearance.99

**Neuromuscular blockers**

The non-depolarizing muscle relaxant rocuronium should be dosed based on IBW which results in a similar time to adequate intubation conditions, while minimizing the duration of action.100 Similarly, rocuronium should also be dosed by ideal body weight.101 Conversely, in order to achieve optimal intubating conditions with the depolarizing relaxant succinylcholine TBW should be used for dosing.102

**Volatile anesthetics**

Volatile anesthetic uptake is determined in part by solubility of the inhaled agent, which is confounded by the increased fat stores in obese patients. Therefore, it would be expected that recovery from relatively insoluble volatile agents would be more rapid than from soluble agents which is what was demonstrated when the less soluble desflurane was compared to sevoflurane in morbidly obese patients undergoing gastric bypass surgery that was supplemented with epidural analgesia.103 However, in another comparative study of sevoflurane vs. desflurane in morbidly obese patients without the use of epidural analgesia there was no difference in recovery.104

**Technical considerations**

Complications related to airway management is a major cause of morbidity and mortality related to
anesthesia in the obese population. Obesity is an independent predictor of difficult mask ventilation and difficult laryngoscopy.\(^{87,105-108}\) Additionally, neck circumference and OSA are independent predictors of difficult airway.\(^{109}\) The ASA’s Difficult Airway Algorithm provides a guideline to management of the difficult airway.\(^{109}\) The ASA’s Difficult Airway Algorithm suggests use of techniques such as awake induction, recruitment of additional personnel as well as the immediate availability of additional advanced airway devices, including tracheotomy equipment.\(^{110}\)

Standard operating room tables have a safe weight capacity of approximately 450 lbs. Specific operating tables designed to hold up to 1 000 lbs should be allocated as needed to prevent patient falls and ensure intraoperative safety. Nerve injury is a known complication related to surgery and patient positioning. Studies have demonstrated an increased risk of nerve injury in the obese surgical population.\(^{111-112}\) Venous access is more difficult in this population, making both intravenous line insertion and laboratory blood sampling quite challenging.\(^{113}\)

### Perioperative complications

#### Pulmonary system

Respiratory mechanics are significantly altered in obesity, and these changes are further exacerbated with general anesthesia. These obesity-related changes are characterized by a reduced functional residual capacity (FRC), primarily via reduction in expiratory reserve volume (ERV) resulting in atelectasis and shunt physiology.\(^{114}\) Obesity also results in reduced lung and chest wall compliance, increased lung resistance, reduced oxygenation and increased work of breathing.\(^{115}\) The reduced FRC results in a shorter period of apnea tolerated by obese patients before desaturation.\(^{116}\)

Overweight (BMI > 25) and obese (BMI > 30) patients have also been noted to have an increased incidence of asthma.\(^{117}\) The mechanism for this association is not clear, but may be related to changes in lung mechanics as outlined above, as well as inflammation and immune function.\(^{118}\) These changes in lung volumes increase the likelihood of morbidly obese surgical patients developing pulmonary complications. In a study of postoperative pulmonary events following bariatric surgery, atelectasis and pneumonia were found to be the two leading adverse events, though the overall incidence of pulmonary complications in this group was <1%.\(^{119}\) The presence of metabolic syndrome in these patients further increased the likelihood of pulmonary complications.\(^{119}\) In addition to an increase in atelectasis during general anesthesia and abdominal surgery, morbidly obese patients have persistent atelectasis postoperatively compared to their non-obese counterparts (Fig. 2).\(^{120}\)

A number of strategies has been suggested to reduce the development of atelectasis in obese patients undergoing anesthesia and surgery. One such intervention is the application of positive end-expiratory pressure (PEEP). Pelosi et al found that a PEEP of 10 cm H\(_2\)O resulted in improved oxygenation and compliance in obese patients compared with no PEEP; no improvement was noted with this amount of PEEP in lean surgical patients.\(^{121}\) Preoxygenation with head of bed elevation has been found to prolong the post-apneic time until desaturation occurs.\(^{122}\)

Noninvasive positive pressure ventilation during anesthesia induction followed by an early lung recruitment maneuver following intubation has been demonstrated to improve oxygenation, and this improvement in oxygenation is correlated with

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**Table 3 Pharmacologic concerns in obesity**

<table>
<thead>
<tr>
<th>Concern</th>
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<tbody>
<tr>
<td>Greater than normal amount adipose tissue</td>
</tr>
<tr>
<td>Increased lean body mass (LBW = IBW + 20–30%)</td>
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<tr>
<td>Increased blood volume</td>
</tr>
<tr>
<td>Smaller than normal fraction total body water</td>
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<tr>
<td>Increased cardiac output</td>
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<tr>
<td>Decreased pulmonary function</td>
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<tr>
<td>Increased proteins, free fatty acids</td>
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<tr>
<td>Increased renal blood flow</td>
</tr>
<tr>
<td>Increased glomerular filtration rate</td>
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<td>Abnormal liver function</td>
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an increase in ERC. A meta-analysis of ventilation strategies in obesity found that lung recruitment maneuvers combined with PEEP also improved oxygenation and compliance during the maintenance of anesthesia.

**Cardiovascular system**

Obesity is associated with a number of cardiovascular system comorbidities that may influence perioperative management and outcomes. These comorbidities include atherosclerotic cardiovascular disease, hypertension, cardiomyopathy, pulmonary hypertension, arrhythmias, thromboembolic disease and poor exercise tolerance. However, as noted elsewhere in this review, obesity itself is not associated with an increased incidence of cardiovascular morbidity and in fact, may be protective. An exception may be in patients that are morbidly obese and have additional insulin resistance. For example, in patients undergoing coronary artery bypass grafting (CABG), those with a BMI > 40 did exhibit an increased risk of perioperative myocardial infarction and morbidity. However, a recent report suggested that even in the non-metabolically-deranged obese patient, cardiovascular complications are in fact more likely.

In the most recent authoritative guidelines, the potential for perioperative cardiovascular risk is determined primarily by functional status, rather than the traditional risk factors outlined by the revised cardiac risk index. Furthermore, as discussed elsewhere in this review, the metabolic syndrome is associated with an increased mortality rate after CABG. Thus while obesity is associated with various cardiovascular risk factors, and body habitus may limit functional status, obesity in and of itself is not necessarily a risk factor for perioperative cardiovascular morbidity.

**Venous thromboembolism**

Several studies have reported that obesity is an independent risk factor for perioperative venous thromboembolism (VTE). The already high risk for VTE is further exacerbated with progressively higher BMI, prolonged surgical time, older age, male sex, history of OSA, obesity hypoventilation syndrome and a previous history of VTE. According to the 2013 Clinical Practice guidelines for bariatric surgical patients, it is recommended that VTE prophylaxis, including sequential compression devices and chemoprophylaxis, to be administered perioperatively. The American Society for Bariatric and Metabolic Surgery in association with American Association of Clinical Endocrinologists and The Obesity Society issued guidelines which recommend that all bariatric surgical patients receive mechanical prophylaxis, early ambulation and chemoprophylactic interventions with low molecular weight heparin (LMWH) or unfractionated heparin. However, chemoprophylactic dosing will need to consider that adipose tissue has a lower blood volume than lean tissue; hence, the volume of distribution of heparin will differ in obese patients. Even though heparin dosing requirements do not increase linearly with body weight, the 2012 American College of Chest Physicians guidelines state that weight-based dosing is preferred to fixed dosing in obese patients. In the treatment of VTE the total body weight is used.

**Fig. 2** Comparison of the percentage of pulmonary atelectasis between morbidity obese and non-obese patients at the three study times (before anesthesia induction, after extubation, and 24 h later). *P < 0.05 compared with before induction (within group); #P < 0.05 compared with the control group (between groups). Reprinted with permission from Eichenberger A, et al. Morbid obesity and postoperative pulmonary atelectasis: an underestimated problem. Anesth Analg 2002;95:1788–92.
to calculate the initial bolus dose and infusion rate to achieve a therapeutic PTT with dosing adjusted accordingly.\textsuperscript{140,141} The dose of LMWH should also be adjusted based on total body weight.\textsuperscript{142} It is suggested that in bariatric surgical patients, enoxaparin dose is adjusted as follows: (i) BMI = <50 kg/m\(^2\) – enoxaparin 40 mg BID SQ; (ii) BMI > 50 kg/m\(^2\) – enoxaparin 60 mg BID SQ.\textsuperscript{143,144}

**Postoperative cognitive decline**

Both postoperative delirium (POD) as well as postoperative cognitive dysfunction (POCD) results in increased morbidity and even mortality.\textsuperscript{143,146} As risk factors may differ between the encompassed entities of POCD and POD,\textsuperscript{147} there is no consensus regarding a unifying etiology and pathophysiology for the constellation of PCD conditions. Over the last decade investigations have focused on the putative role of neuroinflammation in the development of PCD, and have systematically addressed how pro-inflammatory cytokines and immune cells propagate PCD in animal models.\textsuperscript{148–155} Recently, similar inflammatory changes in surgical patients have been noted.\textsuperscript{156–159}

Obesity is associated with both a low-grade chronic inflammatory state\textsuperscript{160} as well as overactivity of the sympathetic nervous system,\textsuperscript{161} and these may be related because cholinergic stimulation is required to terminate the inflammatory response.\textsuperscript{162} Furthermore obesity increases the risk for the development of diabetes,\textsuperscript{163–165} an insulin-resistant state in which elevated levels of pro-inflammatory cytokines supervene.\textsuperscript{166} As pro-inflammatory cytokines interfere with long-term potentiation, the neurobiologic correlate for learning and memory,\textsuperscript{167,168} it is unsurprising that obesity increases dementia risk by 64%.\textsuperscript{169} Hudetz and colleagues were the first to draw attention to the link between the metabolic syndrome and the increased likelihood for the development of PCD (Table 4).\textsuperscript{170,171} The pathophysiologic basis for the relationship between the metabolic syndrome and exaggerated postoperative cognitive decline have further emphasized the role of unresolved inflammation.\textsuperscript{172,173} Furthermore, obese patients are more likely to develop OSA (considered elsewhere in this review) that has an increased risk for postoperative cognitive decline.\textsuperscript{174}

As obese patients are at increased risk for PCD, the application of ‘Care Bundles,’ designed to reduce the modifiable precipitating factors for delirium, are advocated.\textsuperscript{175–180}

**Wound infection**

Obesity increases the risk of postoperative wound infection. Interrogation of the Veterans Affairs Surgical Quality Improvement Program (VASQIP) database showed that in total joint arthroplasty, a BMI > 40 kg/m\(^2\) is an independent predictor for superficial infection.\textsuperscript{181} Similarly, obese patients undergoing open reduction and internal fixation of distal humeral fractures or total elbow arthroplasty,\textsuperscript{132} total ankle arthroplasty or ankle arthrodesis,\textsuperscript{131} total shoulder arthroplasty\textsuperscript{133} fixation for intertrochanteric femur fractures,\textsuperscript{182} and fixation of a fracture of an ankle\textsuperscript{183} all have an increased incidence of surgical-site infections when compared to non-obese patients undergoing the same surgery. Other non-orthopedic surgeries are also complicated by increased incidence of surgical-site infection in obese patients including abdominal hysterectomy, coronary bypass graft and large bowel surgery.\textsuperscript{184} Morbidly obese patients have 6.5-fold increase in deep sternal wound infection.\textsuperscript{185} Interrogation of the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) database for abdominal surgery showed that obesity and morbid obesity are independently associated with overall surgical-site infections development in clean and clean-contaminated cases.\textsuperscript{186} Further analysis of the same database addressing 16 major cardiovascular, orthopedic and oncologic surgeries showed that morbid obesity significantly increased the odds of wound complications in all surgeries except for pneumonectomy.\textsuperscript{126} A retrospective study on lower extremity vascular surgery also found that obesity and morbid obesity were independent predictors of infectious wound complications, including dehiscence, surgical-site infections, seroma and hematoma at 30 days.\textsuperscript{187}
The pathophysiologic mechanisms leading to surgical wound infections in obese patients could include relative hypoperfusion/ischemia, dysregulated immune and inflammatory responses, coupled with decreased delivery of antibiotics. Furthermore, tension on the wound edges is often increased in obese patients resulting in decreased oxygen supply to the wound. Hypovascularity and the difficulty that obese patients have of repositioning themselves may increase the risk of pressure ulcers or pressure-related injuries. Also, redundant skin folds serve as a moist area for micro-organisms to thrive, which may lead to infection and tissue breakdown, and the skin to skin friction may cause ulceration. Adipose tissue macrophages produce excessive cytokines (TNF-alpha, IL-1, IL-6, IL-8, IL-10) and chemokines (IL-8, MCP-1, IP-10, MCP, monocyte chemoattractant protein-1; IP-10 interferon-gamma-inducible protein 10) that act as endocrines, while impaired peripheral blood mononuclear cell function and decreased lymphocyte proliferation significantly disrupt the innate immune response. Apart from these local events, obesity can be associated with other comorbidities including diabetes, anxiety and depression that result in impaired wound healing through impaired immune response.

Strategies designed to mitigate the high likelihood of surgical-site infections include weight-adjusted antibiotics dosing, the use of minimally invasive approaches when possible, and layered closure of incisions.

**Critical care considerations**

The care of the critically ill obese surgical patient requires a number of special considerations. For example, technical aspects related to positioning, monitoring, and vessel cannulation can all be challenging due to increased body habitus. As discussed above, drug-dosing in the obese patient also deserves special consideration given changes in drug distribution and clearance. The data for pharmacokinetic-guided dosing in obese patients are quite limited. Commonly used drugs in the ICU that may require additional consideration include antibiotics, sedative/analgesics and anticoagulants.
Acute respiratory distress syndrome
A recent meta-analysis of BMI and acute respiratory distress syndrome (ARDS) found that obese patients have lower mortality, as noted in our discussion of the Obesity Paradox. Despite mechanical changes associated with obesity in healthy patients, as outlined above, obese patients with ARDS show no additional changes in lung elastance or recruitment ability. Furthermore, obese patients do not fare worse than normal weight patients with ARDS on ECMO, and obesity is not a contraindication for ECMO initiation. When choosing ventilator settings for obese patients, the tidal volume should be based on ideal and not total body weight. The addition of PEEP improves alveolar recruitment and oxygenation in morbidly obese anesthetized postoperative patients.

Proning in obesity
Prone position has been shown to improve mortality in patients with severe ARDS. Given the technical difficulties associated with achieving prone positioning in the obese population, the utility of this intervention in obese patients with ARDS has been questioned. One retrospective review found that proning in patients with abdominal obesity increased risk of mortality, renal failure, hepatic failure. However, another case-controlled study found that proning improves oxygenation and mortality in morbidly obese patients with ARDS compared with non-obese patients with ARDS. A difference in the definition of obesity may account for differing conclusions, as the first study focused on abdominal obesity, as determined by sagittal abdominal diameter on imaging, and the latter determined obesity based on traditional BMI (see elsewhere).

Nutrition
Nutritional support of critically ill obese patients is a necessary component of recovery, as obesity does not mitigate the development of acute ICU-related malnutrition. The recommendations from American Society of Parenteral and Enteral nutrition include early enteral nutrition, as for all patients with critical illness. Caloric requirements should be determined by indirect calorimetry and protein requirements determined by weight-based calculations and urine nitrogen to achieve positive nitrogen balance. The nutritional goal for obese patients can be achieved with high-protein, hypocaloric feeding.

Conclusion
Perioperative care of the obese surgical patient remains a challenging proposition because of the metabolic, pharmacologic, and system-wide disorders that are the foundational basis for the complications that can ensue. In order to understand the Obesity Paradox, in which complication rates may actually be lower than normal weight surgical patients, it will be necessary to distinguish ‘healthy’ obesity from those obese states in which insulin resistance comes to the fore. Further surrogate biomarkers that characterize the different types of obesity will be needed to focus particular attention on those obese surgical patients for whom the perioperative period is particularly hazardous.

Conflict of interest statement
The authors have no potential conflicts of interest.

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