Critical care of the bariatric patient

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Objective: **To synthesize the current literature on care of obese, critically ill, and bariatric surgical patients.**

Data Source: **A MEDLINE/PubMed search from 1966 to August 2005 was conducted using the search terms *obesity*, *bariatric surgery*, and *critical illness*, and a search of the Cochrane Library was also conducted.**

Data Extraction and Synthesis: **An increase in both the prevalence of obesity and the number of bariatric procedures performed has resulted in an increased number of obese and, specifically, bariatric surgical patients who require intensive care unit care. Obesity is a chronic inflammatory state with resultant effects on immune, metabolic, respiratory, cardiovascular, gastrointestinal, hematologic, and renal function. Principles of care of the critically ill obese patient are reviewed and then applied to critically ill bariatric surgical patients. Pharmacotherapy, vascular access, and the presentation and management of both pressure-induced rhabdomyolysis and anastomotic failure after bariatric surgery are also reviewed.**

Conclusions: **Obesity causes a range of pathologic effects on all major organ systems. Knowledge of these effects and issues specific to the intensive care unit care of bariatric patients can help to predict and manage complications in this population. (Crit Care Med 2006; 34:1796–1804)**

KEY WORDS: obesity; obesity surgery; bariatric surgery; intensive care unit; critically ill patients; perioperative risk; mortality

Obesity has emerged as a major public health epidemic in the United States (1). At the turn of the millennium, over one half of Americans were overweight (body mass index [BMI] of $\geq$25 kg/m^2), over 30% were obese (BMI of $\geq$30 kg/m^2), and >5% were morbidly obese (BMI of $\geq$40 kg/m^2) (2–4). The prevalence of obesity in America continues to increase exponentially and is substantially greater than that of other developed countries (5, 6). Obesity is a leading cause of preventable death in the United States, resulting in >100,000 excess deaths per year (7) and an estimated annual cost of $70 billion, accounting for nearly 10% of national health care expenditures (8).

The numerical growth of the obese population has been matched by an increase in the number of obese patients requiring both hospitalization and intensive care unit (ICU) care. Furthermore, the exponential increase in the number of bariatric procedures annually (9–11) suggests that bariatric surgical patients will constitute an ever-increasing portion of obese patients who require ICU care. A knowledge of three fundamental issues is necessary to manage effectively this rapidly growing patient demographic: 1) the pathophysiology of obesity, 2) the response of the obese patient to critical illness, and 3) the postoperative care of the critically ill bariatric patient.

METHODS

A MEDLINE/PubMed search from 1966 to December 2005 was conducted using the National Library of Medicine MeSH search terms *obesity*, *bariatric surgery*, and *critical illness*. These terms were also used to search the Cochrane Library Database. All publication types, languages, and subsets were searched. Relevant studies, case reports, review articles, editorials, short communications, and chapters from selected textbooks were then extracted and manually cross-referenced. Only studies using explicit definitions of obesity or morbid obesity were included. Throughout the review, obesity is defined as a BMI of $\geq$30 kg/m^2 and morbid obesity as a BMI of $\geq$40 kg/m^2, unless specified otherwise. Studies pertaining to critical illness included an ICU length of stay (LOS) of $\geq$24 hrs. Bariatric operations included were adjustable gastric banding, gastroplasty, gastric bypass, and biliopancreatic diversion with duodenal switch.

Although the focus on this review is critical care of the bariatric surgical patient, much of our understanding of obesity and of the response of the obese patient to critical illness does not come directly from this patient population. However, an appreciation of the fundamental physiologic derangements associated with obesity is paramount to caring for bariatric surgical patients. We have thus structured our review as follows. We begin by reviewing the prevalence and consequences of obesity in critical illness. We then adopt a systems-based approach in describing the available data on care of the critically ill obese patient. We end by combining these data with principles of care of the postoperative bariatric patient to make recommendations as to the care of the bariatric surgical patient during critical illness. In many instances, data are available for one demographic group but not the other, and care is taken to make this distinction clear throughout the review.

Prevalence of Obesity in Critical Illness

Within medical-surgical ICUs, the current prevalence of obesity ranges from 9% to 26% (12–14) and that of morbid obesity from 1.4% to 7% (14–16). Recently, Neville et al. (17) reported that 63 of 242 blunt trauma patients (26%) requiring ICU care were obese. A substantial portion of bariatric surgical patients may require prolonged ICU care. Nguyen et al. (18) reported in their randomized trial that 7.6% of laparoscopic gastric bypass patients and 21.1% of open gastric bypass patients re-

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quired ICU care after surgery. Similarly, recent series have documented that 6% to 24% of bariatric surgical patients require >24 hrs of ICU care (19–21).

Obesity and the Risk of Mortality in Critical Illness

Compared with nonobese patients, obese individuals harbor an increased overall mortality (7, 22–27), perioperative mortality (28–30), and mortality after trauma (17, 31–33). However, in studies of critically ill patients, the effect of BMI on reported outcomes is mixed. Ray et al. (14) conducted a prospective cohort study of 2,148 adult patients admitted to a medical ICU between January 1997 and August 2001. No significant differences were observed between BMI groups (normal weight, overweight, obese, and morbidly obese) with respect to ICU LOS, hospital LOS, or mortality. Other large series of medical-surgical ICU patients have also not found an association between obesity and increased mortality (16, 34). However, Goulenok et al. (12) noted in a prospective study of 813 medical ICU patients that obese patients (defined as BMI of ≥27) had a significantly increased ICU LOS (4 days vs. 3 days, respectively; $p = .024$) and mortality (32% vs. 13%, respectively; $p < .001$) compared with nonobese patients. El-Solh et al. (15) performed a retrospective review of 117 morbidly obese patients and 132 nonobese controls admitted to two medical ICUs over a 7-yr period. Compared with nonobese patients, morbidly obese patients had a significantly increased LOS (17.7 days vs. 11.3 days, $p = .007$) and ICU LOS (9.3 days vs. 5.8 days, $p = .007$). In-hospital mortality in obese ICU patients was nearly double that of nonobese controls (30% vs. 17%, $p = .019$). Another case-control study matched 170 obese, ventilated patients with 170 ventilated, nonobese controls in a medical-surgical ICU (13). Obesity was an independent risk factor for ICU death, with a reported odds ratio of 2.1 (95% confidence interval, 1.2–3.6; $p < .007$).

Several factors may account for these observed discrepancies. Under-recording of data necessary to calculate BMI, inaccurate estimations of these data, failure to adjust body mass for fluid balance, and failure to control for race, socioeconomic status, and obesity-related co-morbidities may all confound the relationship between BMI and outcomes in critical illness. Future studies employing rigorous methodology are warranted.

Far less information is available as to the course of bariatric surgical patients requiring ICU care. In a retrospective review of 250 patients undergoing either vertical banded gastroplasty or gastric bypass, Helling et al. (19) noted that hospital LOS doubled for those patients requiring >24 hrs of ICU care after surgery. Factors predictive of ICU admission after bariatric surgery are shown in Table 1 (19, 35, 36).

Table 1. Risk factors for intensive care unit admission after bariatric surgery

Male sex
Age of >50 yrs
Body mass index of >60 kg/m^2
Diabetes mellitus
Cardiovascular disease
Obstructive sleep apnea syndrome
Venous stasis
Intraoperative complications

Pathophysiology of Obesity

Inflammation, hypercoagulability, and insulin resistance characterize obesity as a disease process that mimics critical illness. Adipose tissue is a potent source of tumor necrosis factor-α and interleukin-6. Neutrophils of obese patients have impaired chemotaxis and activation (37). Increased concentrations of fibrinogen and plasminogen activator inhibitor-1 and decreased concentration of antithrombin-III and decreased fibrinolysis are found in obese patients (38). Thus, obesity is a chronic inflammatory state that diminishes both immune and metabolic reserves. Increased BMI requires increased cardiovascular, respiratory, and metabolic work, resulting in a markedly diminished physiologic reserve. Major physiologic derangements associated with obesity are outlined below and summarized in Table 2.

Pulmonary. Obesity results in a restrictive lung pattern due to both increased pulmonary blood volume (39, 40) and increased chest wall mass from adipose tissue (40). Abnormal diaphragm position, upper airway resistance, and increased daily CO_2 production exacerbate respiratory load and further increase the work of breathing (41–43). The consequences of this restrictive pattern are decreased functional residual capacity, vital capacity, total lung capacity, inspiratory capacity, minute ventilatory volume, and expiratory reserve volume. Patients may also exhibit an obesity-related obstructive air flow pathology that manifests itself as an increased ratio of forced expiratory volume in 1 sec to forced vital capacity (FEV_1:FVC) (42).

Obesity is strongly correlated with obstructive sleep apnea syndrome, a condition characterized by repetitive partial or complete obstruction of the upper airway that is associated with arterial blood oxygen desaturations and arousals from sleep (44, 45). A decreased respiratory rate and ultimately periods of apnea occur frequently, with resultant self-limited periods of severe hypoxia (46). Associated symptoms include snoring, systemic and pulmonary hypertension, nocturnal angina, sleep-related cardiac dysrhythmias, gastroesophageal reflux disease, insomnia, polycythemia, and daytime somnolence (47, 48). In rare instances, sudden death from sinus arrest may occur (49). Apneic episodes occur with greatest frequency during rapid eye movement sleep (50), which, in turn, usually does not resume until the third to fifth night after surgery (51).

Table 2. Major organ-system derangements in obesity

Organ System	Pathology
Respiratory	↓ FRC, TLC, VC, IC, ERV
	↑ FEV_1/FVC
	Obstructive sleep apnea syndrome
Cardiovascular	↑ Blood volume
	↑ Vascular tone
	↓ Ventricular contractility
Renal	↑ Clearance of renally excreted drugs
	Hypertensive and diabetic nephropathy
Hematologic	↑ Fibrinogen
	↑ PAI-1
	↓ AT-III
	Venous stasis
Gastrointestinal	Hiatal hernia
	↑ Gastric secretion volume
	↓ Gastric pH
Metabolic/Endocrine	↑ Resting energy expenditure
	Insulin resistance
	↑ Proteolysis
Immunologic	↑ TNF-α
	↑ IL-6
	Impaired neutrophil function

↓, decreased; FRC, functional residual capacity; TLC, total lung capacity; VC, vital capacity; IC, inspiratory capacity; ERV, expiratory reserve volume; ↑, increased; FEV_1/FVC, ratio of forced expiratory volume in one second to forced vital capacity; PAI-1, plasminogen activator inhibitor-1; AT-III, antithrombin-III; TNF-α, tumor necrosis factor-α; IL-6, interleukin-6.

Preexisting pulmonary disease in obese patients leads to an increased prevalence of postoperative pulmonary complications (28, 52, 53). Obese patients' relatively short, wide necks and redundant oropharyngeal tissue make elective intubation difficult. Effective preoxygenation is not possible, and rapid arterial desaturation is common after induction of anesthesia. The use of a laryngeal mask airway may prove invaluable in cases of difficult endotracheal intubation. Postoperatively, splinting and atelectasis may further diminish pulmonary reserve. A review of 24,157 postanesthesia care unit patients revealed that obese patients were more than twice as likely to suffer from a critical respiratory event defined as unanticipated hypoxemia, hypoventilation, or upper airway obstruction requiring an active intervention (52).

An understanding of the altered respiratory mechanics secondary to obesity is crucial to managing postoperative bariatric patients. Early ambulation and minimal time spent in the supine position while in bed should be stressed. Ambulation within 2 hrs of surgery and frequently thereafter is common to many postoperative bariatric protocols (35).

El-Solh et al. (15) noted that morbidly obese patients fare worse once pulmonary complications develop. Compared with nonobese controls, morbidly obese patients spent significantly more time on the ventilator (10.6 days vs. 4.6 days, $p = .0004$), required more time to achieve extubation (3.2 days vs. 1.8 days, $p = .009$), and required more oxygen throughout hospitalization (F_{IO_2} of 38.4% vs. 31.1%, $p < .001$).

An increased prevalence of hiatal hernia and increased intraabdominal pressure secondary to large abdominal panniculus are believed to augment the risk of aspiration in the obese population (53). Altered gastric pH and fluid volume have been found in obese surgical patients. In a cross-sectional study by Vaughan et al. (54), 42 of 56 of obese patients (75%) compared with 0 of 50 normal weight controls (0%) shared the combination of gastric secretion volume of >25 mL and pH of <2.5, levels considered traditionally (albeit, somewhat arbitrarily) to place the adult patient at risk for aspiration pneumonitis (55). However, Zacchi et al. (56) found normal gastroesophageal junction resistance gradients in obese patients without gastroesophageal reflux disease or hiatal hernia and concluded that obesity alone was not a risk factor for aspiration. In light of these incomplete data, it is prudent to take precautions against acid aspiration in the critically ill obese patient. Specifically, histamine H_2-antagonists maintain gastric volume of <25 mL and gastric pH of >2.5 effectively in morbidly obese patients (57).

Mechanical ventilation for the obese patient with respiratory failure is challenging. Delivered tidal volume should be calculated based on ideal body weight (IBW) rather than actual body weight (ABW) to avoid high airway pressures, alveolar overdistention, and barotrauma. End-tidal CO_2 monitors are unreliable because of widened alveolar-arterial gradients present in most obese patients (58). Providing an intubated, morbidly obese patient with 10 cm of positive end-expiratory pressure improves lung volumes, Pa_{O_2}, Pa_{CO_2}, elasticity, pressure-volume curves, and intraabdominal pressure compared with nonobese controls (59). Finally, the reverse Trendelenburg position at 45 degrees facilitates liberation from the ventilator and extubation by improving ventilatory mechanics, as described above. In a population of critically ill obese patients, the reverse Trendelenburg positioning at 45 degrees resulted in increased Pa_{O_2} and tidal volume and decreased respiratory rate as compared with the supine position (60).

A substantial fraction of bariatric patients may require >24 hrs of mechanical ventilation postoperatively. Helling et al. (19) reported that 44 of 250x consecutive bariatric surgery patients degrees remained intubated for >24 hrs after surgery. Prolonged respiratory failure after bariatric surgery, however, seems to be rare. Livingston et al. (36) reported only 9 of 1,067 cases (0.6%) of respiratory failure in their series of gastric bypass patients. Furthermore, using the 2002 Healthcare Cost and Utilization Project National Inpatient Sample, Poulose et al. (61) documented 7.3 cases of respiratory failure per 1,000 bariatric patients.

Patients with respiratory failure may benefit from early tracheostomy (62, 63). Tracheostomy is hazardous and technically demanding in obese patients because of the aforementioned cervical anatomy. Longer tracheostomy tubes with sharper angles may be necessary to accommodate increased neck girth in obese patients (64, 65). Percutaneous tracheostomy remains controversial for these patients. Mansharamani et al. (66) reported no complications in 13 consecutive obese patients, but Byhahn et al. (67) reported a 2.7-fold increased risk of perioperative complications in obese patients compared with nonobese controls (95% confidence interval, 1.8–4.1; $p < .001$), with a 4.9-fold increased risk of serious complications (95% confidence interval, 3.1–7.8; $p < .001$). The overall complication rate of percutaneous tracheostomy for 73 obese patients was 43.8%.

The prevalence of obstructive sleep apnea syndrome in large series of bariatric surgical patients is 39% (36) to 71% (67). Polysomnography is recommended for preoperative evaluation of bariatric surgical patients. Empirical continuous positive airway pressure (CPAP) via mask (10 cm H_2O) may be instituted if patients are unable to complete polysomnography before surgery (68). The CPAP acts to displace the tongue and pharyngeal soft tissues, preventing airway obstruction. Although CPAP may cause gastric distention from ingested air at increased pressure, CPAP has not been found to increase the rate of anastomotic failure. In a series of 1,067 consecutive gastric bypass patients, Livingston et al. (36) noted similar rates of anastomotic leak in patients receiving CPAP (2 of 159 patients, 1.3%) compared with those not receiving CPAP (10 of 908 patients, 1.3%).

Cardiovascular. Obesity is a risk factor for coronary artery disease that is independent from the influences of diabetes mellitus and hypertension (69). Sixty percent of obese patients have hypertension, which resolves with weight loss (70–72). Due to a usually sedentary lifestyle, symptoms of angina or congestive heart failure may not be elicited easily.

The pathophysiology of cardiovascular disease related to obesity involves an increase in both preload and afterload. Approximately 3 mL of blood volume are needed per 100 g of adipose tissue (73); as BMI increases, so does circulating blood volume. Increased blood volume increases preload, stroke volume, cardiac output, and myocardial work (74, 75). Elevated circulating concentrations of catecholamines, mineralocorticoids, renin, and aldosterone serve to increase afterload (76). Hyperkinesis, myocardial hypertrophy, decreased compliance, diastolic dysfunction, and eventually ventricular failure ensue (74, 77, 78). Sudden death from cardiac arrhythmias or sinus arrest can occur (77).

The diastolic dysfunction characteristic of obesity results in poor fluid tolerance. A pulmonary artery catheter may be useful in obese patients who require large-volume fluid resuscitation. Noninvasive blood pressure monitoring by cuff sphygmomanometer is often inaccurate due to size discrepancy; therefore, an indwelling arterial catheter should be employed when hemodynamic stability is in question. Finally, although the use of perioperative β-blockade in patients at risk for cardiovascular disease decreases morbidity and mortality from cardiovascular events (79), β-blockade should be used cautiously for obese patients because of impaired ventricular contractility due to decreased β-adrenergic receptors (80, 81).

Both CO_2 pneumoperitoneum and reverse Trendelenburg positioning have been implicated in impairing cardiac function during laparoscopic gastric bypass (82). In a recent trial, Nguyen et al. (83) randomized 51 patients to receive either open or laparoscopic gastric bypass. Both groups were placed in the reverse Trendelenburg position. Abdominal insufflation in the laparoscopic group resulted in increased systemic vascular resistance and decreased cardiac output compared with both baseline and the open gastric bypass group immediately after incision. However, systemic vascular resistance and cardiac output recovered within 1.5 hrs and 2.5 hrs of abdominal insufflation, respectively, in the laparoscopic group, and no adverse sequelae were noted. Transient hypercarbia was controlled effectively through ventilator manipulations.

Reverse Trendelenburg positioning during bariatric surgery likely has a small effect on cardiac dynamics (82). In the aforementioned study by Nguyen et al. (83), cardiac output increased significantly after incision in open

gastric bypass patients despite being placed in the reverse Trendelenburg position.

Nutrition. Malnutrition and obesity are not mutually exclusive, and the supposition that "starving" obese patients during critical illness is well tolerated or even beneficial is erroneous. Obese patients have an increased resting energy expenditure secondary to increased BMI, with central adipose tissue being more metabolically active than peripheral adipose tissue (84).

Obesity is characterized by the "metabolic X syndrome": insulin resistance, hyperinsulinemia, hyperglycemia, coronary artery disease, hypertension, and hyperlipidemia (85). Substrate overload leads to baseline resistance to pancreatic polypeptides. Elevated basal insulin concentrations in obesity suppress lipid mobilization from body stores, causing accelerated proteolysis to support gluconeogenesis, which in turn forces rapid loss of muscle mass and early deconditioning. A case-control study of obese blunt trauma patients revealed that obese patients mobilized relatively more protein and less fat compared with nonobese controls (86). This shift from fat to carbohydrate metabolism increases the respiratory quotient and may cause hypercarbia and impede extubation.

The enhanced metabolic rate, accelerated net protein breakdown, and alterations in lipid and carbohydrate metabolism of critical illness exacerbate these preexisting metabolic derangements. Nutrition in critically ill obese patients should thus supply enough glucose to spare protein. Calories should be supplied primarily as carbohydrates, with fats given to prevent essential fatty acid deficiency (87). Most recommended enteral feeding regimens supply 30 kcal/kg and 2.0 g/kg protein per day, based on IBW (41, 58, 88). However, recent data have reported improved outcomes using hypocaloric feedings. Dickerson et al. reviewed 40 critically ill, obese surgical patients and found that those who received hypocaloric enteral feedings (<20 kcal $\cdot$ kg^{-1} $\cdot$ day^{-1} based on IBW) had decreased ICU LOS, received fewer days of antibiotics, and decreased length of mechanical ventilation compared with those fed eucaloric feedings (≥ 20 kcal $\cdot$ kg^{-1} $\cdot$ day^{-1}) (89). The authors postulated that improved outcome in the hypocaloric group was related to fewer complications of overfeeding. Prospective trials are warranted.

Total parenteral nutrition is used often in postoperative bariatric patients when enteral feeding is impossible. However, although data specifically addressing the bariatric patient population are not available, total parenteral nutrition has not been shown to decrease major postoperative complication rates or mortality in critically ill postoperative patients (90, 91). Placement of a feeding gastrostomy tube at the time of surgery should be considered when a prolonged period of critical illness is anticipated.

Thromboembolic Disease. Obese patients are believed to be at increased risk of thromboembolic complications due to increased blood viscosity, decreased concentration of antithrombin-III, and increased concentration of both fibrinogen and plasminogen activator inhibitor-1 produced by adipose tissue (38, 92). Sedentary lifestyle, venous stasis, and pulmonary hypertension augment this risk (92–94). Endothelial injury as a result of surgery constitutes the final element of Virchow's triad (hypercoagulability, stasis, endothelial injury) (95), priming the obese surgical patient for perioperative thromboembolic complications.

Several prospective studies of patients have identified obesity as a risk factor for postoperative venous thromboembolism (VTE) after elective major abdominal surgery (94, 96, 97). Two large autopsy series revealed that 67% (98) and 75% (99) of patients with no preexisting risk factors who died of acute pulmonary thromboembolism were obese.

Despite an increased risk within the obese population, the reported prevalence of VTE after bariatric surgery is low. Prospective studies have reported a rate of VTE from 0% to 2.4% and of pulmonary embolism from 0% to 1.2% (19, 100–107). However, variable methods of prophylaxis were used, and the majority of patients were not critically ill.

Although VTE is rare, pulmonary embolism is the most common cause of postoperative mortality (19, 108) and an independent risk factor for death after bariatric surgery (106). In a review of 3,464 bariatric surgery patients, pulmonary embolism accounted for 50% of deaths (105). Livingston et al. (36) documented nine postoperative pulmonary emboli in 1,067 bariatric surgery patients, of which six were fatal.

Whereas >95% of obesity surgeons use some form of thromboprophylaxis routinely (109), no specific regimen is employed universally. Scholton et al. (110) documented a low rate of postoperative VTE with a multiple-modality prophylaxis protocol including early ambulation, graded compression stockings, intermittent pneumatic compression stockings and enoxaparin at 40 mg subcutaneously every 12 hrs. A recent meta-analysis recommended unfractionated heparin, low molecular weight heparin, or intermittent pneumatic compression stockings for high-risk patients undergoing elective abdominal surgery (111). Emphasis must be placed on proper timing of prophylaxis, with the initial dose of pharmacoprophylaxis given 1–2 hrs preoperatively.

Prophylactic inferior vena cava filter placement may be beneficial for those bariatric patients at extremely high risk for postoperative VTE. A higher prevalence of VTE has been reported in super obese (BMI of >50 kg/m^2 (2)) patients, patients with truncal obesity, venous stasis disease, or a history of VTE (107, 112, 113). Although no randomized trials addressing the value of prophylactic inferior vena cava filter placement in this population exist, new retrievable inferior vena cava filters may be considered before surgery for patients with one or more of these high-risk factors.

Pharmacology. Obese patients with normal renal function have an increased glomerular filtration rate and thus an increased clearance of drugs excreted by the kidney (114, 115). However, diabetes mellitus and hypertension, which complicate obesity frequently, may cause renal dysfunction. Therefore, renal function must be determined on an individual basis. Further, calculated and measured creatinine clearance correlate poorly in obesity (116), mandating measurement of creatinine clearance with timed urine specimens in all obese patients with suspected renal dysfunction.

An increased ratio of adipose to lean body mass alters the volume of distribution (V_d) of lipophilic drugs. Accumulation of lipophilic drugs in adipose tissue not only increases the dose necessary to gain effect, but also prolongs the elimination half-life (117, 118). Dosing of these drugs in obese patients is generally approximated best using ABW rather than IBW (119). Conversely, the V_d of hydrophilic drugs in general relates better to lean body mass (approximated by IBW) because of poor penetration into adipose tissue. Dosing of hydrophilic drugs based on ABW in the obese patient population may grossly overestimate necessary dosages, leading to toxicity (120). However, blood, extracellular fluid, body organ, and connective tissue volume, to which hydrophilic drugs may distribute, are all also increased in obese patients (121). Thus, whereas dosing of hydrophilic drugs should initially be based on IBW, serum concentrations should be monitored whenever possible to ensure therapeutic concentrations (122, 123).

Due to variable alterations in V_d, clearance, and elimination half-life, dosing adjustments for specific drugs in obese patients can be complex. Individual drugs used commonly in critical illness that have been studied in obese patients are discussed below.

Propofol is a hypnotic, lipophilic drug with a rapid onset and short duration of action (124). Both V_d and clearance of propofol are increased in obese patients and correlate with ABW (125). Elimination half-life is unchanged compared with nonobese controls. Dosing of propofol for both induction and maintenance of anesthesia should thus be based on ABW.

The lipophilic benzodiazepines demonstrate markedly increased V_d, similar clearance, and increased elimination half-life in obese patients (126). Based on these data, single dosing of benzodiazepines in obese patients (e.g., premedication for bedside procedures) should be calculated based on ABW to account for the increased V_d of the drug (127). However, dose calculations for continuous infusion in obese patients should follow IBW because clearance is not significantly different from nonobese patients. Frequent interruptions in infusion with assessment of patient response are necessary to avoid delayed liberation from the ventilator and prolonged ICU LOS (128).

Fentanyl is a synthetic, lipophilic opioid with a rapid onset of action and minimal his-

Table 3. Dosing weights in obese patients for selected drugs used commonly in critical illness

Drug	Dosing Weight
Propofol	ABW
Benzodiazepines	
Single-dosage	ABW
Continuous infusion	IBW
Fentanyl	$52/(1 + [196.4 \times e^{-0.025\ ABW} - 53.66]/100)$
Vancomycin	ABW
Aminoglycosides	IBW + (0.40 × [ABW − IBW])
Fluoroquinolones	IBW + (0.40 × [ABW − IBW])
Drotrecogin alfa (activated)	ABW

ABW, actual body weight; IBW, ideal body weight.

tamine-related vasodilation (129). Bently et al. (130) found similar pharmacokinetics of fentanyl in obese and nonobese patients, suggesting dosing based on IBW. Shibutani et al. (131) reported a poor linear correlation between the fentanyl dose required for analgesia and total body weight. They derived a correction factor (Table 3) for the weight-based dosing of fentanyl in the postoperative period, termed "pharmacokinetic mass," that correlated well with fentanyl dose over a range of 48–181 kg.

Although the pharmacokinetics of many antimicrobials in obese patients remain largely unknown, several exceptions warrant discussion. Both the V_d and clearance of vancomycin correlate better with ABW than IBW in morbidly obese patients (132, 133). Shorter elimination half-life of vancomycin relative to nonobese patients (mean of 3.3 hrs vs. 7.2 hrs, $p < .0001$) may require shorter dosing intervals to achieve therapeutic steady-state trough concentrations (e.g., every 8 hrs vs. every 12 hrs) (133). Due to variability in both dosage amount and dosage interval, serum concentrations of vancomycin should be monitored in obese patients (134).

Linezolid is an oxazolidinone with activity against multi–drug-resistant Gram-positive bacteria (135, 136). Stein et al. (137) measured serum concentrations of linezolid in seven obese patients with cellulitis treated with a standard dosing regimen (600 mg by mouth every 12 hrs for 12 days). Although mean serum concentrations were decreased compared with nonobese controls, prolonged *in vitro* serum inhibitory activity was observed against two of three clinical isolates of methicillin-resistant *Staphylococcus aureus* and one clinical isolate of vancomycin-resistant *Enterococcus faecium*. Clinical cure was achieved in all subjects.

The hydrophilic aminoglycosides and fluoroquinolones require use of a predetermined dosing weight correction factor to calculate dosing weight (Table 3).

Clinical studies suggest a dosing weight correction factor of approximately 0.45 for both aminoglycosides (138) and quinolones (139). However, because a wide range of dosing weight correction factors for aminoglycosides have been reported in the literature (140–142), subsequent dosing should be based on serum concentrations. Monitoring serum concentrations of aminoglycosides is particularly important in obesity because of an increased susceptibility to nephrotoxicity (143, 144). Alterations of dosage interval in obese patients with normal renal function are usually unnecessary (122, 145). Once-daily dosing of aminoglycosides in obese patients has not been studied and is not recommended.

The PROWESS trial of drotrecogin alfa (activated) (146) excluded patients weighing >135 kg. A subsequent study that included morbidly obese patients (range, 59–227 kg) documented similar plasma concentrations and elimination half-lives of drotrecogin alfa (activated) when dosed by ABW (147). Therefore, drotrecogin alfa (activated) may be used for treatment of severe sepsis in morbidly obese patients and should be dosed according to ABW without limitation of dosage. Dosing weights in obese patients for drugs used commonly in critical illness are summarized in Table 3.

Vascular Access. Gaining central venous access in obese patients is made difficult by obscured anatomic landmarks, increased depth of insertion necessary to gain venipuncture, and a distorted angle of insertion. Gilbert et al. (148) demonstrated increased success of cannulation, decreased need to resort to an alternative technique, and significantly fewer complications for internal jugular vein cannulation in a mixed population of obese and coagulopathic ICU patients. Vigilant surveillance for catheter-related infections is necessary as central catheters are usually kept indwelling longer in critically ill obese patients (15), and intertriginous folds predispose to infection.

Anastomotic Leak After Bariatric Surgery. Anastomotic leak is a rare but deadly complication after bariatric surgery. Recent case series have reported a prevalence ranging from 0.5% to 2% (20, 36, 105, 107). Bariatric patients who sustain a postoperative anastomotic leak have increased hospital LOS, ICU LOS, and mortality (106, 149).

In a recent review of 210 consecutive laparoscopic Roux-en-Y gastric bypass patients, Hamilton et al. (149) found severe tachycardia (heart rate, ≥120 beats/min) and respiratory failure (the development of an increasing oxygen requirement after discharge from the postanesthesia care unit, SaO_2 of <92% on room air, or respiratory rate of ≥24 breaths/min) to be the two most common presenting manifestations of anastomotic leak. Eight of nine patients (89%) with anastomotic leaks experienced severe tachycardia and six of nine patients (67%) experienced respiratory distress. By multivariate analysis, both respiratory distress (odds ratio, 6.0; 95% confidence interval, 2.57–208.5; $p < .01$) and severe tachycardia (odds ratio, 23.2; 95% confidence interval, 1.2–29.4; $p < .05$) were independent predictors of anastomotic leak. Failure of progression to extubation or sudden respiratory decompensation in the immediate postoperative period should thus raise suspicion of intraabdominal pathology. Concurrent symptoms and findings, such as left shoulder pain, increasing abdominal pain, a perception of impending doom, or an isolated left pleural effusion on chest radiograph may aid in differentiating anastomotic leak from other common causes of postoperative respiratory decline, most notably pulmonary embolism (108). Whereas upper gastrointestinal contrast imaging is both useful and employed routinely in diagnosing anastomotic failure, a negative study does not exclude the diagnosis; a water-soluble gastrointestinal contrast study revealed an anastomotic leak in only two of nine patients (22%) in the aforementioned study by Hamilton et al (149).

Failure to recognize an anastomotic leak can result in rapid deterioration and death. All postoperative bariatric patients with persistent tachycardia and respiratory distress in whom pulmonary embolism has been ruled out should thus undergo exploratory laparotomy. Most morbidly obese patients exceed the weight limitation for the gantry of computed tomography scanners, precluding the use of computed tomography to image the abdomen.

Pressure-Induced Rhabdomyolysis. Pressure-induced rhabdomyolysis is a rare but well-described postoperative complication that results from prolonged, unrelieved pressure to muscle during surgery (150–153). Major risk factors include prolonged operative time and obesity. Rhabdomyolysis after bariatric surgery may affect the lower limbs, gluteal, or lumbar regions (154–157). In a recent review, mean operating room time, mean BMI (67 kg/m^2 vs. 56 kg/m^2), and the prevalence of diabetes mellitus were significantly greater in patients who developed rhabdomyolysis (155). Prevention of rhabdomyolysis and related complications includes attention to padding and positioning on the operating table, minimization of operative time, and maintenance of a high index of suspicion postoperatively.

Although the most common clinical presentation of rhabdomyolysis is numbness and muscular pain, patients may lack symptoms due to perioperative epidural anesthesia. Cutaneous eruptions (e.g., purpura, epidermolysis) over sites of muscle injury have been de-

scribed (158). Muscle breakdown leads to the release of intracellular myoglobin and creatine phosphokinase. Myoglobinuria is suspected in the presence of brown urine and confirmed by a positive urine dipstick test for hemoglobin in the absence of erythrocytes on urinalysis (159). Elevated creatine phosphokinase concentrations peak on the second to fifth postoperative day and usually resolve within 2 wks of surgery (154).

Patients suspected of having rhabdomyolysis should be monitored in the ICU. Treatment is instituted once the creatine phosphokinase concentration increases to >5,000 IU/L, including aggressive hydration and diuresis with mannitol to a target urine output of 1.5 $mL \cdot kg^{-1} \cdot hr^{-1}$. Mannitol mobilizes muscular interstitial fluid and increases renal tubular flow (160). Alkalization of urine with sodium bicarbonate increases the solubility of myoglobin in a pH-dependent manner (161).

Compartment syndrome, acute renal failure, and mortality may complicate rhabdomyolysis. Acute renal failure (prevalence, 50% (159)) results from hypovolemia, tubular obstruction, acidosis, and free radical release (162). Factors predictive of renal failure in rhabdomyolysis include age of >70 yrs, serum creatine phosphokinase concentration of >16,000 IU/L, degree of hypoalbuminemia, and sepsis (163). Fortunately, complete recovery of tubular function is the norm, albeit after a variable period of renal replacement therapy (151). Hemofiltration has the added advantage of rapid clearance of myoglobin.

CONCLUSION

Obese patients, many of whom are now bariatric surgical patients, constitute an increasing percentage of critically ill patients. Obesity is characterized by a chronic proinflammatory state, changes in cellular immunity, hypercoagulability, and insulin resistance. These baseline physiologic derangements, coupled with the stress of critical illness, present unique challenges to the critical care team. Knowledge of the pathophysiology of obesity and of the presentation and treatment of serious complications of bariatric surgery are necessary to manage these patients effectively. Prospective data addressing critically ill, bariatric patients are scant. Trials that include and examine morbidly obese surgical patients are needed.

REFERENCES

1. The Surgeon General's Call to Action to Prevent and Decrease Overweight and Obesity. Rockville, MD, Public Health Service, Office of the Surgeon General, 2001
2. Mokdad AH, Bowman BA, Ford ES, et al: The continuing epidemics of obesity and diabetes in the United States. *JAMA* 2001; 286:1195–1200
3. Must A, Spadano J, Coakley EH, et al: The disease burden associated with overweight and obesity. *JAMA* 1999; 282:1523–1529
4. Hedley AA, Ogden CL, Johnson CL, et al: Prevalence of overweight and obesity among US children, adolescents, and adults, 1999–2002. *JAMA* 2004; 291: 2847–2850
5. Flegal KM, Carroll MD, Kuczmarski RJ, et al: Overweight and obesity in the United States: Prevalence and trends, 1960–1994. *Int J Obes* 1998; 22:39–47
6. VanItalie TB: Prevalence of obesity. *Endocrinol Metab Clin North Am* 1996; 25: 887–905
7. Flegal KM, Graubard BI, Williamson DF, et al: Excess deaths associated with underweight, overweight, and obesity. *JAMA* 2005; 293:1861–1867
8. Colditz GA: Economic costs of obesity and inactivity. *Med Sci Sports Exerc* 1999; 31: S663–S667
9. Schirmer B, Watts SH: Laparoscopic bariatric surgery. *Surg Endosc* 2004; 18: 1875–1878
10. Santry HP, Gillen DL, Lauderdale DS: Trends in bariatric surgical procedures. *JAMA* 2005; 294:1909–1917
11. Trus TL, Pope GD, Finlayson SR: National trends in utilization and outcomes of bariatric surgery. *Surg Endosc* 2005; 19: 616–620
12. Goulenok C, Monchi M, Chiche JD, et al: Influence of overweight on ICU mortality. *Chest* 2004; 125:1441–1445
13. Bercault N, Boulain T, Kuteifan K, et al: Obesity-related excess mortality rates in an adult intensive care unit: A risk-adjusted matched cohort study. *Crit Care Med* 2004; 32:998–1003
14. Ray DE, Matchett SC, Baker K, et al: The effect of body mass index on patient outcomes in a medical ICU. *Chest* 2005; 127: 2125–2131
15. El-Solh A, Sikka P, Bozkanat E, et al: Morbid obesity in the medical ICU. *Chest* 2001; 120:1989–1997
16. Tremblay A, Bandi V: Impact of body mass index on outcomes following critical care. *Chest* 2003; 123:1202–1207
17. Neville AL, Brown CV, Weng J, et al: Obesity is an independent risk factor of mortality in severely injured blunt trauma patients. *Arch Surg* 2004; 139:983–987
18. Nguyen NT, Goldman C, Rosenquist J, et al: Laparoscopic versus open gastric bypass: Randomized study of outcomes, quality of life, and costs. *Ann Surg* 2001; 234:279–291
19. Helling TS, Willoughby TL, Maxfield DM, et al: Determinants of the need for intensive care and prolonged mechanical ventilation in patients undergoing bariatric surgery. *Obes Surg* 2004; 14:1036–1041
20. Yeats M, Wedergren S, Fox N, et al: The use and modification of clinical pathways to achieve specific outcomes in bariatric surgery. *Am Surg* 2005; 71:152–154
21. Cendan JC, Abu-aouf D, Gabrielli A, et al: Utilization of intensive care resources in bariatric surgery. *Obes Surg* 2005; 15: 1247–1251
22. Drenick EJ, Gurunanjappa SB, Seltzer F, et al: Excessive mortality and causes of death in morbidly obese men. *JAMA* 1980; 243: 443–445
23. Harris T, Cook EF, Garrison R, et al: Body mass index and mortality among nonsmoking older persons: The Framingham Heart Study. *JAMA* 1988; 259:1520–1524
24. Garrison RJ, Castelli WP: Weight and thirty-year mortality of men in the Framingham Study. *Ann Intern Med* 1985; 103: 1006–1009
25. Troiano RP, Frongillo EA Jr, Sobal J, et al: The relationship between body weight and mortality: A quantitative analysis of combined information from existing studies. *Int J Obes Relat Metab Disord* 1996; 20:63–75
26. Fontaine KR, Redden DT, Wang C, et al: Years of life lost due to obesity. *JAMA* 2003; 289:187–193
27. Calle EE, Thun MJ, Petrelli JM, et al: Body-mass index and mortality in a prospective cohort of U.S. adults. *N Engl J Med* 1999; 341:1097–1105
28. Pasulka PS, Bistrian BR, Benotti PN, et al: The risks of surgery in obese patients. *Ann Intern Med* 1986; 104:540–546
29. Prem KA, Mensheha NM, McKelvey JL: Operative treatment of adenocarcinoma of the endometrium in obese women. *Am J Obstet Gynecol* 1965; 92:16–24
30. Postlethwait RW, Johnson WD: Complications following surgery for duodenal ulcer in obese patients. *Arch Surg* 1972; 105: 438–440
31. Choban PS, Weireter LJ, Maynes C: Obesity and increased mortality in blunt trauma. *J Trauma* 1991; 31:1253–1257
32. Arbabi S, Wahl W, Hemmila M, et al: The cushion effect. *J Trauma* 2003; 54: 1090–1093
33. Byrnes MC, McDaniel MD, Moore MB, et al: The effect of obesity on outcomes among injured patients. *J Trauma* 2005; 58: 232–237
34. Garrouste-Orgeas M, Troche G, Azoulay E, et al: Body mass index: An additional prognostic factor in ICU patients. *Intensive Care Med* 2004; 30:437–443
35. Davidson JE, Callery C: Care of the obese patient requiring intermediate-level care or intensive care. *Obes Surg* 2001; 11:93–97
36. Livingston EH, Huerta S, Arthur D, et al: Male gender is a predictor for morbidity and age a predictor of mortality for patients undergoing bypass surgery. *Ann Surg* 2002; 236:576–582
37. Cottam DR, Schaefer PA, Fahmy D, et al: The effect of obesity on neutrophil Fc receptors and adhesion molecules (CD16, CD11b, CD622L). *Obes Surg* 2001; 12: 230–235

38. Juhan-Vague MCA: Regulation in fibrinolysis in the development of atherothrombosis: Role of adipose tissue. *Thromb Haemost* 1999; 82:832–836
39. Luce JM: Respiratory complications of obesity. *Chest* 1980; 78:626–631
40. Pelosi P, Croci M, Ravagnan I, et al: Total respiratory system, lung, and chest wall mechanics in sedated-paralyzed postoperative morbidly obese patients. *Chest* 1996; 109: 144–151
41. Levi D, Goodman ER, Patel M, et al: Critical care of the obese and bariatric surgical patient. *Crit Care Clin* 2003; 19:11–32
42. Ray C, Sue D, Bray G, et al: Effects of obesity on respiratory function. *Am Rev Respir Dis* 1983; 128:501–506
43. Suratt P, Wilheit S, Hsiao H: Compliance of the chest wall in obese subjects. *J Appl Physiol* 1984; 57:403–409
44. Gibson GJ: Obstructive sleep apnoea syndrome: Underestimated and undertreated. *Br Med Bull* 2004; 72:49–64
45. Strobel RJ, Rosen RC: Obesity and weight loss in obstructive sleep apnea: A critical review. *Sleep* 1996; 19:104–115
46. Fletcher EC, Shah Anjana, Qian W, et al: "Near miss" death in obstructive sleep apnea: A critical care syndrome. *Crit Care Med* 1991; 19:1158–1164
47. Adams JP, Murphy PG: Obesity and anesthesia and intensive care. *Br J Anaesth* 2000; 85:91–108
48. Sleep-related breathing disorders in adults: Recommendations for syndrome definitions and measurement techniques in clinical research. The Report of the American Academy of Sleep Medicine Task Force. *Sleep* 1999; 22:677–689
49. Gilleminault C, Connoly SJ, Winkle RA: Cardiac arrhythmia and conduction disturbances during sleep in 400 patients with sleep apnea syndrome. *Am J Cardiol* 1983; 52:490–494
50. Murphy PG: Obesity. *In*: Foundations of Anaesthesia: Basic and Clinical Sciences. Hemmings HC Jr, Hopkins PM (Eds). London, Mosby, 2000, pp 703–711
51. Knill RL, Moote CA, Skinner MI, et al: Anesthesia with abdominal surgery leads to intense REM sleep during the first postoperative week. *Anesthesiology* 1990; 73: 52–61
52. Rose DK, Cohen MM, Wigglesworth DF, et al: Critical respiratory events in the postanesthesia care unit. *Anesthesiology* 1994; 81: 410–418
53. Shenkman Z, Shir Y, Brodsky JB: Perioperative management of the obese patient. *Br J Anaesth* 1993; 70:349–359
54. Vaughan RW, Bauer S, Wise L: Volume and pH of gastric juice in obese patients. *Anesthesiology* 1975; 43:686–689
55. Roberts RB, Shirley MA: Reducing the risk of acid aspiration during cesarean section. *Anesth Analg* 1974; 53:859–868
56. Zacchi P, Mearin F, Humbert P, et al: Effect of obesity on gastroesophageal resistance to flow in man. *Dig Dis Sci* 1991; 36: 1473–1480
57. Vila P, Valles CJ, Canet J, et al: Acid aspiration in morbidly obese patients: Famotidine vs. ranitidine. *Anaesthesia* 1991; 46: 967–969
58. El-Solh AA: Clinical approach to the critically ill, morbidly obese patient. *Am J Respir Crit Care Med* 2004; 169:557–561
59. Pelosi P, Ravagnan I, Giurati G, et al: Positive end-expiratory pressure improves respiratory function in obese but not in normal subjects during anesthesia and paralysis. *Anesthesiology* 1999; 91: 1221–1231
60. Burns SM, Egloff MB, Ryan B, et al: Effect of body position on spontaneous respiratory rate and tidal volume in patients with obesity, abdominal distention and ascites. *Am J Crit Care* 1994; 3:102–106
61. Poulose BK, Griffen MR, Zhu Y, et al: National analysis of adverse patient safety events in bariatric surgery. *Am Surg* 2005; 71:406–413
62. Pivalizza EG: Obesity and airway control. *Anaesth Intensive Care* 1994; 22:315–316
63. McLear PW, Thawley SE: Airway management in obesity hypoventilation syndrome. *Clin Chest Med* 1991; 12:585–588
64. Sugerman HJ: Pulmonary function in morbid obesity. *Gastroenterol Clin North Am* 1987; 16:225–237
65. Headley WB, Rodning CB: Fabricated single lumen tracheal cannula for a morbidly obese patient. *J Otolaryngol* 1993; 22: 438–441
66. Mansharamani NG, Koziel H, Garland R, et al: Safety of bedside percutaneous dilatational tracheostomy in obese patients in the ICU. *Chest* 2000; 117:1426–1429
67. Byhahn C, Lischke V, Meninger D, et al: Peri-operative complications during percutaneous tracheostomy in obese patients. *Anaesthesia* 2005; 60:12–15
68. Frey WC, Pilcher J: Obstructive sleep-related breathing disorders in patients evaluated for bariatric surgery. *Obes Surg* 2003; 13:676–683
69. Hubert HB, Feinleib M, McNamara PM, et al: Obesity as an independent risk factor for cardiovascular disease: A 26-year follow-up of participants in the Framingham Heart Study. *Circulation* 1983; 67:968–977
70. Alexander JK, Peterson KL: Cardiovascular effects of weight reduction. *Circulation* 1972; 45:310–318
71. Alpert MA, Lambert CR, Panayiotou H, et al: Relation of duration of morbid obesity to left ventricular mass, systolic function, and diastolic filling, and effect of weight loss. *Am J Cardiol* 1995; 76:1194–1197
72. Kochar MS: Hypertension in obese patients: *Postgrad Med* 1993; 93:193–200
73. Alexander JK: The cardiomyopathy of obesity. *Prog Cardiovasc Dis* 1985; 27:325–333
74. Backman L, Freyschuss U, Hallbert D, et al: Cardiovascular function in extreme obesity. *Acta Med Scand* 1983; 149:437–439
75. Berklap B, Cesur V, Corapcioglu D, et al: Obesity and left ventricular diastolic dysfunction. *Int J Cardiol* 1995; 52:23–26
76. Reisen E, Frohlich ED, Messerli FN, et al: Cardiovascular changes after weight reduction in obesity hypertension. *Ann Intern Med* 1983; 98:315–319
77. Messerli FH: Cardiovascular effects of obesity and hypertension. *Lancet* 1982; 1:1165–1168
78. Alport MA, Hashimi MW: Obesity and the heart. *Am J Med Sci* 1993; 306:117–123
79. Mangano DT, Layug EL, Wallace A, et al: Effect of atenolol on mortality and cardiovascular morbidity after noncardiac surgery. *N Engl J Med* 1996; 335:13–20
80. Merlino G, Scaglione R, Carrao S, et al: Association between reduced lymphocyte beta-adrenergic receptors and left ventricular dysfunction in young obese subjects. *Int J Obes Metab Disord* 1994; 18:699–703
81. Merlino G, Scaglione R, Paterna S, et al: Lymphocyte beta-adrenergic receptors in young subjects with peripheral or central obesity: Relationship with central haemodynamics and left ventricular function. *Eur Heart J* 1994; 15:786–792
82. Nguyen NT, Wolfe BM: The physiologic effects of pneumoperitoneum in the morbidly obese. *Ann Surg* 2005; 241:219–226
83. Nguyen NT, Ho HS, Fleming NW, et al: Cardiac function during laparoscopic vs. open gastric bypass: A randomized comparison. *Surg Endosc* 2002; 16:78–83
84. Azevedo A, Ramos E, von Hafe P, et al: Upper-body adiposity and risk of myocardial infarction. *J Cardiovasc Risk* 1999; 6:321–325
85. Bray GA: Pathophysiology of obesity: *Am J Clin Nutr* 1992;55:488S–494S
86. Jeevanandam M, Young DH, Schiller WR: Obesity and the metabolic response to severe trauma in man. *J Clin Invest* 1991; 87:262–269
87. Ireton-Jones CS, Francis C: Obesity: Nutrition support and practice and application to critical care. *Nutr Clin Pract* 1995; 10: 144–149
88. Marik P, Varon J: The obese patient in the ICU. *Chest* 1998; 113:492–498
89. Dickerson RN, Boschert KJ, Kudsk KA, et al: Hypocaloric enteral tube feeding in critically ill obese patients. *Nutrition* 2002; 18: 241–246
90. Perioperative total parenteral nutrition in surgical patients. The Veterans Affairs Total Parenteral Nutrition Cooperative Study Group. *N Engl J Med* 1991;325:525–532
91. Heyland DK, MacDonald S, Keefe L, et al: Total parenteral nutrition in the critically ill patient. *JAMA* 1998; 280:2013–2019
92. Batist G, Bothe A, Bern M, et al: Low antithrombin III in morbid obesity: Return to normal with weight reduction. *JPEN J Parenter Enteral Nutr* 1983; 7:447–449
93. Merli GJ: Prophylaxis for deep venous thrombosis and pulmonary embolism in the surgical patient. *Clin Cornerstone* 2000; 2:15–28

94. Clayton JK, Anderson JR, McNicol GP: Preoperative prediction of postoperative deep venous thrombosis. *BMJ* 1976; 2:910–912
95. Virchow RKL: Gesammele abhandlungen zue wissenschaftlicher medizin, von meidinger sohn. *Franfur-ann-main* 1856
96. Kakkar VV, Howe CT, Nicolaides AN, et al: Deep vein thrombosis of the leg: Is there a "high risk" group? *Am J Surg* 1970; 120: 527–530
97. Lowe GD, AcArdle BM, Carter DC, et al: Prediction and selective prophylaxis of venous thrombus in elective gastrointestinal surgery. *Lancet* 1982; 1:409–412
98. Blaszyk H, Wollan PC, Witkiewicz AK, et al: Death from pulmonary thromboembolism is severe obesity: Lack of association with established genetic and clinical risk factors. *Virchows Arch* 1999; 434:529–532
99. Blaszyk H, Bjornsson J: Factor V Leiden and morbid obesity in fatal postoperative pulmonary embolism. *Arch Surg* 2000; 135: 1410–1413
100. Westling A, Bergqvist D, Bostrom A, et al: Incidence of deep venous thrombosis in patients undergoing obesity surgery. *World J Surg* 2002; 26:470–473
101. Printen KJ, Miller EV, Mason EE, et al: Venous thromboembolism in the morbidly obese. *Surg Gynecol Obstet* 1978; 147: 63–64
102. Holmes NJ, Brolin RE, Kaufman JL: Is morbid obesity a risk factor for postoperative venous thromboembolism? *Infect Med* 1994; 11:273–278
103. Erikkson S, Backman L, Ljungstrom KG: The incidence of clinical postoperative thrombosis after gastric surgery for obesity during 16 years. *Obes Surg* 1997; 7:332–335
104. Gonzalez QH, Tishler DS, Plata-Munoz JJ, et al: Incidence of clinically significant deep venous thrombosis after laparoscopic Roux-en-Y gastric bypass. *Surg Endosc* 2004; 18:1082–1084
105. Podnos YD, Jimenez JC, Wilson SE, et al: Complications after laparoscopic gastric bypass. *Arch Surg* 2003; 138:957–961
106. Fernandez AZ, Demaria EJ, Tichansky DS, et al: Multivariate analysis of risk factors for death following gastric bypass for treatment of morbid obesity. *Ann Surg* 2004; 239: 698–703
107. Mason EE, Renquist KE, Jiang D: Perioperative risks and safety of surgery for severe obesity. *Am J Clin Nutr* 1992;55:573S–576S
108. Brolin RE: Complications of surgery for severe obesity. *Prob Gen Surg* 2000; 17:55–61
109. Wu EC, Barba CA: Current practices in the prophylaxis of venous thromboembolism in bariatric surgery. *Obes Surg* 2000; 10:7–14
110. Scholton DJ, Hoedema RM, Scholten SE: A comparison of two different prophylactic dose regimens of low molecular weight heparin in bariatric surgery. *Obes Surg* 2002; 12:19–24
111. Gerts WH, Heit JA, Clagett GP, et al: Prevention of venous thromboembolism. *Chest* 2001;119:132S–175S
112. Sugerman HJ, Sugerman EL, Wolke L, et al: Risks and benefits of gastric bypass in morbidly obese patients with severe venous stasis disease. *Ann Surg* 2001; 234:41–46
113. Sapala JA, Wood MH, Schuhknecht MP, et al: Fatal pulmonary embolism after bariatric operations for morbid obesity: A 24-year retrospective analysis. *Obes Surg* 2003; 13: 819–825
114. Salazar DE, Corcoran GB: Predicting creatinine clearance and renal drug clearance in obese patients from estimated fat-free body mass. *Am J Med* 1988; 84:1053–1060
115. Stockholm KH, Brochner-Mortensen J, Hoilund-Carlson PF: Increased glomerular filtration rate and adrenocortical function in obese women. *Int J Obes* 1980; 4:57–63
116. Snider RD, Kruse JA, Bander JJ, et al: Accuracy of estimated creatinine clearance in obese patients with stable renal function in the intensive care unit. *Pharmacotherapy* 1995; 15:747–753
117. Baile GR, Cockshott ID, Douglas EJ, et al: Pharmakinetics of propofol during and after long-term continuous infusion for maintenance of sedation in ICU patients. *Br J Anaesth* 1992; 68:486–491
118. Trempy GA, Rock P: Anesthetic management of a morbidly obese woman with a massive ovarian cyst. *J Clin Anesth* 1993; 5:62–68
119. Morgan DJ, Bray KM: Lean body mass as a predictor of drug dosage: Implications for drug therapy. *Clin Pharmacokinet* 1994; 26:292–307
120. Abernethy DR, Greenblatt DJ: Pharmacokinetics of drugs in obesity. *Clin Pharmacokinet* 1982; 7:108–124
121. Naeye RL, Roode P: The size and numbers of cells in visceral organs in human obesity. *Am J Clin Path* 1970; 54:251–253
122. Cheymol G: Clinical pharmacokinetics of drugs in obesity: An update. *Clin Pharmacokinet* 1993; 25:103–114
123. Yee JY, Duffull SB: The effect of body weight on dalteparin pharmacokinetics. *Eur J Clin Pharmacol* 2000; 56:293–297
124. Nasraway SA: Use of sedative medications in the intensive care unit. *Semin Respir Crit Care Med* 2001; 22:165–174
125. Servin F, Farinotti R, Haberer JP, et al: Propofol infusion for maintenance of anesthesia in morbidly obese patients receiving nitrous oxide: A clinical and pharmacokinetic study. *Anesthesia* 1993; 78:657–665
126. Greenblatt DJ, Abernethy DR, Locniskar A, et al: Effect of age, gender, and obesity on midazolam kinetics. *Anesthesia* 1984; 61: 27–35
127. Casati A, Putzu M: Anesthesia in the obese patient: Pharmacokinetic considerations. *J Clin Anesth* 2005; 17:134–145
128. Kress JP, Pohlman AS, O'Connor MF, et al: Daily interruption of sedative infusions in critically ill patients undergoing mechanical ventilation. *N Engl J Med* 2000; 342: 1471–1477
129. Shapiro BA, Warren J, Egol AB, et al: Practice parameters for intravenous analgesia and sedation for adult patients in the intensive care unit: An executive summary. Society of Critical Care Medicine. *Crit Care Med* 1995; 23:1596–1600
130. Bently JB, Borel JD, Gillespie TJ, et al: Fentanyl pharmacokinetics in obese and nonobese patients. Abstr. *Anesthesiology* 1981; 55:A177
131. Shibutani K, Inchiosa MA, Sawada K, et al: Pharmacokinetic mass of fentanyl for postoperative analgesia in lean and obese patients. *Br J Anaesth* 2005; 93:377–383
132. Bauer LA, Black DJ, Lill JS: Vancomycin dosing in morbidly obese patients. *Eur J Clin Pharmacol* 1998; 54:621–625
133. Blouin RA, Bauer LA, Miller DD, et al: Vancomycin pharmacokinetics in normal and morbidly obese subjects. *Antimicrob Agents Chemother* 1982; 21:575–580
134. Beardon DT, Rodvold KA: Dosing adjustment for antibacterials in obese patients: Applying clinical pharmacokinetics. *Clin Pharmacokinet* 2000; 38:415–426
135. Stalker DJ, Jungbluth GL, Hopkins NK, et al: Pharmacokinetics and tolerance of single and multiple-dose oral or intravenous linezolid, an oxazolidinone antibiotic, in healthy volunteers. *J Antimicrob Chemother* 2003; 51:1239–1246
136. Kutscha-Lissberg F, Helber U, Muhr G, et al: Linezolid penetration into bone and joint tissues infected with methicillin-resistance staphylococci. *Antimicrob Agents Chemother* 2003; 47:3964–3966
137. Stein GE, Schooley SL, Peloquin CA, et al: Pharmacokinetics and pharmacodynamics of linezolid in obese patient with cellulitis. *Ann Pharmacother* 2005; 39:427–432
138. Traynor AM, Nafziger AN, Bertino JS: Aminoglycoside dosing weight correction factors for patients of various body sizes. *Antimicrob Agents Chemother* 1995; 39: 545–548
139. Allard S, Kinzig M, Bovin G, et al: Intravenous ciprofloxacin disposition in obesity. *Clin Pharmacol Ther* 1993; 54:368–373
140. Bauer LA, Edwards WAD, Dellinger EP, et al: Influence of weight on aminoglycoside pharmacokinetics in normal weight and morbidly obese patients. *Eur J Clin Pharmacol* 1983; 24:643–647
141. Blouin RA, Brouwer KL, Record KE, et al: Amikacin pharmacokinetics in morbidly obese patients undergoing gastric-bypass surgery. *Clin Pharmacokinet* 1985; 4:70–72
142. Korsager S: Administration of gentamicin to obese patients. *Int J Clin Pharmacol Ther Toxicol* 1980; 18:549–553
143. Corcoran GB, Salazar DE, Scgentag JJ: Excessive aminogylcoside nephrotoxicity in obese patients. *Am J Med* 1988; 85:279
144. Corcoran GB, Salazar DE: Obesity as a risk factor in drug-induced organ injury: IV. Increased gentamicin nephrotoxicity in the obese overfed rat. *J Pharmacol Exp Ther* 1989; 248:17–22

145. Wurtz R, Itokazu G, Rodvold K: Antimicrobial dosing in obese patients. *Clin Infect Dis* 1997; 25:112–118
146. Bernard GR, Vincent J, Laterre P, et al: Efficacy and safety of recombinant human activated protein C for severe sepsis. *N Engl J Med* 2001; 344:699–709
147. Levy H, Small D, Heiselman DE, et al: Obesity does not alter the pharmacokinetics of drotrecogin alfa (activated) in severe sepsis. *Ann Pharmacother* 2005; 39:262–267
148. Gilbert TB, Seneff MG, Becker RB: Facilitation of internal jugular venous cannulation using an audio-guided Doppler ultrasound vascular access device: Results from a prospective, dual-center, randomized, crossover clinical study. *Crit Care Med* 1996; 24:2053–2058
149. Hamilton EC, Sims TL, Hamilton TT, et al: Clinical predictors of leak after laparoscopic Roux-en-Y gastric bypass for morbid obesity. *Surg Endosc* 2003; 17:679–684
150. Bertrand M, Godet G, Fléron M, et al: Lumbar muscle rhabdomyolysis after abdominal aortic surgery. *Anesth Analg* 1997; 85: 11–15
151. Tuckey J: Bilateral compartment syndrome complicating prolonged lithotomy position. *Br J Anaesth* 1996; 77:546–549
152. Bildsten SA, Dmochowski RR, Spindel MR, et al: The risk of rhabdomyolysis and acute renal failure with the patient in the exaggerated lithotomy position. *J Urol* 1994; 152:1970–1972
153. Guzzi LM, Mills LA, Greenman P: Rhabdomyolysis, acute renal failure, and the exaggerated lithotomy position. *Anesth Analg* 1993; 77:635–637
154. Gorecki PJ, Cottam D, Ger R, et al: Lower extremity compartment syndrome following a laparoscopic Roux-en-Y gastric bypass. *Obes Surg* 2002; 12:289–291
155. Bostanjian D, Anthone GJ, Hamoui N, et al: Rhabdomyolysis of gluteal muscles leading to renal failure: A potentially fatal complication of surgery in the morbidly obese. *Obes Surg* 2003; 13:302–305
156. Wiltshire JP, Custer T: Lumbar muscle rhabdomyolysis as a cause of acute renal failure after Roux-en-Y gastric bypass. *Obes Surg* 2003; 13:306–313
157. Torres-Villalobos G, Kimura E, Mosqueda JL, et al: Pressure-induced rhabdomyolysis after bariatric surgery. *Obes Surg* 2003; 13: 297–301
158. Miyamoto T, Ikehar A, Kobayashi T, et al: Cutaneous eruptions in coma patients with nontraumatic rhabdomyolysis. *Dermatol* 2001; 203:233–237
159. Penn AS: Myoglobinuria. *In*: Myology. Vol. 2. Engel AG, Baker BQ (Eds). New York, McGraw-Hill, 1986, pp 1785–1794
160. Zager RA, Bredi C: The influence of mannitol on myoglobinuric acute renal failure: Functional, biochemical, and morphological assessments. *J Am Soc Nephrol* 1991; 2:848–855
161. Abassi ZA, Hoffman A, Better OS: Acute renal failure complicating muscle crush injury. *Semin Nephrol* 1998; 18:558–565
162. Vanholder R, Sever MS, Erek E, et al: Rhabdomyolysis. *J Am Soc Nephrol* 2000; 11: 1553–1561
163. Ward MM: Factors predictive of acute renal failure in rhabdomyolysis. *Arch Intern Med* 1988; 148:1553–1557