

Preoperative preparation and premedication of bariatric surgical patient

ABSTRACT

The prevalence of obesity has tripled worldwide over the past four decades. The United States has the highest rates of obesity, with 88% of the population being overweight and 36% obese. The UK has the sixth highest prevalence of obesity. The problem of obesity is not isolated to the developed world and has increasingly become an issue in the developing world as well. Obesity carries an increased risk of many serious diseases and health conditions, including type 2 diabetes, heart disease, stroke, sleep apnea, and certain cancers. Our ability to take care of this population safely throughout the perioperative period begins with a thorough and in-depth preoperative assessment and meticulous preparation. The preoperative assessment begins with being able to identify patients who suffer from obesity by using diagnostic criteria and, furthermore, being able to identify patients whose obesity is causing pathologic and physiologic changes. A detailed and thorough anesthesia assessment should be performed, and the anesthesia plan individualized and tailored to the specific patient's risk factors and comorbidities. The important components of the preoperative anesthesia assessment and patient preparation in the patient suffering from obesity include history and physical examination, airway assessment, medical comorbidities evaluation, functional status determination, risk assessment, preoperative testing, current weight loss medication, and review of any prior weight loss surgeries and their implications on the upcoming anesthetic. The preoperative evaluation of this population should occur with sufficient time before the planned operation to allow for modifications of the preoperative management without needing to delay surgery as the perioperative management of patients suffering from obesity presents significant practical and organizational challenges.

Key words: Ambulatory surgery in the obese patient, anesthesia considerations in the obese patient, obesity, pathophysiology of obesity, perioperative evaluation of the obese

Introduction

Obesity is a preventable medical disease that has increased significantly worldwide in the past few decades. According to the World Health Organization, worldwide obesity has nearly tripled since 1975.^[1] The report states that:

- 39% of adults aged 18 years and over were overweight in 2016 and 13% were obese.
- Over 340 million children and adolescents aged 5-19 were overweight or obese in 2016.
- 39 million children under the age of 5 were overweight or obese in 2020.

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- Most of the world’s population lives in a country, where overweight and obesity kills more people than underweight.

The Centers for Disease Control and Prevention (CDC) reports^[2]:

- In 2017-2018, the prevalence of patients suffering with obesity in the United States was 42.4%.
- From 1999 –2000 through 2017 –2018, US obesity prevalence increased from 30.5% to 42.4%. During the same time, the prevalence of severe obesity increased from 4.7% to 9.2%.
- Severe obesity is expected to affect 23.4% of non-Latino white adults, 24.5% of Latino adults, and 31.7% of non-Latino black Americans.
- In the United States, nearly 1 in 4 adults are expected to have severe obesity by 2030 (24.2%; 95% CI, 22.9 to 25.5), and the prevalence will be higher than 25% in 25 states.^[3]

In 2005, the estimated overall obesity prevalence in Saudi Arabia was reported as 35.5%.^[4] In 2020, Althumiri *et al.*^[5] reported that the prevalence of obesity in Saudi Arabia had fallen to 24.7%. Although Saudi Arabia has a decreasing trend in obesity prevalence, which is in stark contrast to the rise being seen across the world, it is important to note that still nearly 1 in 4 adults in the study sample were obese.

There are approximately 234 million major surgeries performed each year around the world. About 48.3 million surgical and nonsurgical procedures are done in the United States each year, out of which 228,000 are bariatric surgical procedures.^[6]

The UK National Health System’s (NHS) official statistics on obesity in 2020 revealed that hospital admissions directly attributable to obesity vary between 8% and 33% per 100,000 population. The same report lists a national admission rate for bariatric surgeries as 13% per 100,000 population.

With the projected increase in the rate of obesity, it is reasonable to assume that more than one-third of the adult surgical patients will be affected by obesity. Obesity is associated with increased risk of many serious diseases and health conditions, including type 2 diabetes, heart disease, stroke, sleep apnea, and certain cancers. Our ability to guide this population safely through the perioperative period begins with a thorough and in-depth preoperative assessment and preparation.

Definition, Diagnostic Criteria, and Pathophysiology

The Obesity Medicine Association defines obesity as “a chronic, relapsing, multi-factorial, neurobehavioral disease, wherein an increase in body fat promotes adipose tissue

dysfunction and abnormal fat mass physical forces, resulting in adverse metabolic, biomechanical, and psychosocial health consequences. Here are a variety of obesity subtypes, with the most significant groups being:

- Morbid obesity/metabolically abnormal obese (MAO): a condition commonly defined as a body mass index (BMI) of above 40 kg/m²
- Metabolically healthy obesity (MHO): obesity without metabolic syndrome
- Normal-weight obesity: individuals with normal BMI who may still have elevated body fat content and therefore be at increased risk for metabolic comorbidities.^[7]

There are several anthropometric and body composition techniques used to determine the body fat composition, each having their own advantages and disadvantages. Considering convenience, relative accuracy, and cost, the most commonly used method of determining obesity is the BMI, a calculation easily computed using height and weight (weight [kg]/height [m]²; see Table 1). The major limitation to BMI, though, is that the calculation does not differentiate between adipose and non-adipose tissue on an individual level. Since a body could be heavier due to muscle mass, the calculation can overestimate fat content in a person with a higher muscle mass. Furthermore, BMI also differs with ethnicity.^[7] Therefore, it cannot diagnose body fat percentage or overall health in an individual. However, BMI does correspond well with total body adiposity at a population level making it a reasonable screening method.^[8] Other commonly used methods of obesity determination are the waist circumference measurement and waist-to-height ratio. These are used to identify abdominal adiposity that is associated with an increased risk of cardiovascular disease in obese patients.^[9] Abdominal adiposity is defined by a waist-to-height ratio >0.5. Like BMI, the results of these measurements also vary specific to the different populations studied, and discrepancies can be found in individuals with higher muscle mass.^[10,11] More sophisticated methods of measuring obesity include scanning techniques like densitometry, dual-energy x-ray absorption (DEXA), computed tomography (CT), and magnetic resource imaging (MRI), along with bioelectrical impedance.

The exact mechanisms of increased adiposity in the development of metabolic disorders are still unclear.

Table 1: Obesity defined according to BMI

	Body mass index (weight [kg]/height [m] ²)
Overweight/Pre-obesity	25-29.9
Obesity class 1	30-34.9
Obesity class 2	35-39.9
Obesity class 3	>40

However, the dysregulated production and secretion of a number of bioactive substances derived by the adipose tissue, known as adipocytokines or adipokines, likely contribute to the obesity-related metabolic diseases. These adipokines, including leptin, resistin, visfatin, retinol-binding protein, cytokines-like tumor necrosis factor α (TNF α), and interleukins like IL-1, IL-6, IL-18, lead to altered glucose and lipid homeostasis, insulin resistance, and an increased inflammatory response.^[12,13]

Perioperative Care of the Obese Patient

The perioperative management of the obese and morbidly obese patients presents significant practical and organizational challenges. A detailed and thorough anesthesia assessment should be performed, and the anesthesia plan individualized and tailored to the specific patient's risk factors and comorbidities.

The preoperative evaluation of the obese patient should occur in sufficient time before the planned operation to allow for modifications of the preoperative management without the need to delay surgery.

When taking care of the obese patient, our task as anesthesiologists remains focused on relevant medical-history-taking, physical examination, appropriate laboratory testing, and perioperative risk analysis. The important components of the preoperative anesthesia assessment in the obese patient include the following:

- History and examination
- Airway assessment
- Medical comorbidities evaluation
- Functional status determination
- Risk assessment
- Preoperative testing
- Venous thromboembolism prophylaxis.

While obesity is associated with many diseases that are relevant to the anesthesia provider [Figure 1],^[14-66] two diseases that have the greatest impact on perioperative management and anesthesia planning are obstructive sleep apnea (OSA) and metabolic syndrome.

OSA

OSA is common in patients suffering with obesity, with 40–90% of them being affected, and it carries a high relevance in the perioperative period.^[67] Patients with OSA have an increased risk of airway obstruction, hypoxia, hypercarbia, and difficult mask ventilation. Furthermore, OSA is often associated with hypertension, increased sensitivity to

the central and peripheral effects of opioids,^[68] altered cardiovascular function, pulmonary hypertension, and left-ventricular dysfunction.^[69,70]

To diagnose OSA, a polysomnography is needed, but the availability of a validated questionnaire (the STOP-BANG questionnaire) allows for identification of suspected disease. In the obese patient, a score above 3 on the STOP-BANG questionnaire has a sensitivity >90% for detecting OSA with a positive predictive value of 85%. A score above 5 has a sensitivity of 53% and specificity of 70% in predicating moderate-to-severe OSA.^[71] For patients who screen positive, an evaluation of the serum bicarbonate level should be considered. An elevated serum bicarbonate value may indicate carbon dioxide retention and thus an association with sleep-related breathing disorders.^[72]

The arterial blood gas should be considered in the following patients^[73]:

- Patients with obesity and strong suspicion for obesity hypoventilation syndrome (OHS) scheduled for moderate- to high-risk surgeries
- Peripheral oxygen saturation <95%
- Forced vital capacity <3 L or forced expiratory volume in 1 s <1.5 L
- Presence of wheezes at rest
- Serum bicarbonate levels above 27 mEq/L.

Patients who are on continuous positive airway pressure (CPAP)/bilevel positive airway pressure (BiPAP) therapy should continue with positive airway pressure assistance preoperatively to the day of surgery and resume thereafter. The use of noninvasive ventilation preoperatively has been shown to improve cardiac parameters, positively influence the patients respiratory drive, and increase the volume of the pharyngeal space.^[74,75]

For patients diagnosed with severe OSA or OHS, who are not already on CPAP/BiPAP therapy, it is recommended to initiate therapy 4 weeks prior to surgery. CPAP/BiPAP therapy has been shown to attenuate the cardiometabolic abnormalities in this population.^[76] The use of CPAP seems to decrease the postoperative apnea–hypopnea index (AHI) in OSA patients and may reduce the in-hospital length of stay.^[77]

Preoperative respiratory muscle training may be an option to increase inspiratory muscle strength and improve postoperative oxygenation in patients with obesity.^[78] However, the preoperative use of incentive spirometry has not been demonstrated to significantly improve respiratory function after bariatric surgery.^[79]

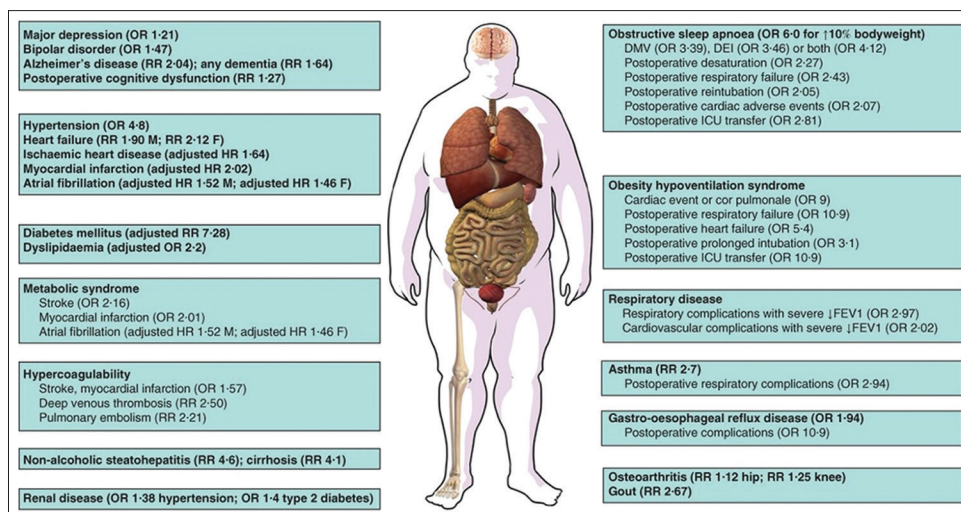


Figure 1: Main obesity-related diseases^[14-66]. Carron M., B. Safaee Fakhri B., G. Ippariello G., *et al.* Perioperative care of the obese patient. *BJS*2020;107:e39-e55 by permission of Oxford University Press

Airway assessment is an important part in the pre-anesthetic evaluation of any patient but becomes even more vital in a patient with obesity. Obesity and increased neck circumference increase the risk of difficult mask ventilation.^[80] Difficult mask ventilation has been reported in 8.8% of patients with obesity and 11% of the morbidly obese population.^[81,82] The predictors of a difficult airway are similar in patients with and without obesity.^[83] Male sex, presence of OSA, and large neck circumference (>40 cm) are the most often reported independent risk factors for a difficult airway in patients with obesity.^[14]

Patients with morbid obesity who are undergoing elective surgery are at a higher risk for regurgitation and pulmonary aspiration when compared to patients without obesity. Preoperative aspiration prophylaxis may decrease gastric volume and increase gastric pH in morbidly obese patients^[84] However, there is no consensus, if morbidly obese patients should get H₂ blockers and/or metoclopramide routinely before surgery.

Moon *et al.*^[85] in a recent narrative review stated that obesity is not an independent risk factor for aspiration and that aspiration occurs because of incorrect aspiration risk assessment or failure to modify the anesthesia technique. The authors encourage the use of gastric perioperative ultrasound in evaluating the quantity of gastric content in patients with obesity.

Metabolic syndrome

Metabolic syndrome is a constellation of medical conditions that commonly manifest together and significantly increase the risk for cardiovascular disease and diabetes mellitus. Metabolic syndrome is not a disease; it is a descriptive clustering of atherosclerotic cardiovascular risk factors.

The prevalence of metabolic syndrome in the US population was estimated to be 34% in the middle of the previous decade. According to the National Cholesterol Education Program (NCEP) criteria, the prevalence of metabolic syndrome in bariatric surgical patients at that time was 80%.^[86]

The average prevalence of metabolic syndrome in patients with obesity is 31% and is associated with a two-fold increase in the risk of coronary heart disease, cerebrovascular disease, and a 1.5-fold increase in the risk of all-cause mortality. Abdominal obesity is the most frequently observed component of metabolic syndrome.^[87] Patients must have three or more of the following five risk factors to be diagnosed with metabolic syndrome: abdominal obesity, high triglycerides, low HDL cholesterol, high blood pressure, and high fasting-glucose levels.^[88]

Criteria for metabolic syndrome

- Insulin resistance: fasting glucose \geq 100 mg/dL
- Blood pressure \geq 130 mmHg/ \geq 85 mm Hg
- Triglycerides >150 mg/dl (1.7 mmol/l)
- Low HDL cholesterol: men <40 mg/dL (1.04 mmol/l)
- Women <50 mg/dL (1.3 mmol/l)
- Abdominal obesity: waist circumference \geq 102 cm (> 40 in) in men
- Waist circumference \geq 88 cm (>35 in) in women.

Surgery patients with obesity and metabolic syndrome have been found to be at an increased risk of mortality, adverse cardiac events, pulmonary complications, acute kidney injury, stroke, wound complications, reintubation, ventilator dependence for longer than 48 hours after surgery, and hyperglycemia during surgical stress leading to an increased risk of surgical site infections.^[66,89-91]

A 5-10% weight loss prior to surgery should be encouraged. Mean weight loss of 7.4 kg has been reported to improve hypertension, hyperlipidemia, and insulin resistance before bariatric surgery.^[92]

Diabetes mellitus is strongly associated with obesity. Patients with poor control of their diabetes are more likely to have wound infections, acute kidney failure, and surgical complications.^[93] A hemoglobin A1C of 6.5 to 7% or less is recommended, although an HbA1C of 7 to 8% can be considered in difficult-to-control diabetics.^[94]

Laboratory testing should be tailored to the individual patient, depending on comorbidities and the type and urgency of surgery. Due to the increased prevalence of cardiovascular risk factors in patients with obesity, like dyslipidemia and impaired fasting-glucose level, routine preoperative screening for these conditions may be considered.^[95] NT-proBNP and BNP levels preoperatively may be beneficial in high-risk patients; the European Society of Cardiology and the European Society of Anesthesiology define this group of patients as having a functional capacity of less than 4 METs (metabolic equivalents) or a revised cardiac risk index greater than 1 for vascular and greater than 2 for non-vascular surgery.^[96]

Preoperative electrocardiogram (ECG) in patients with obesity is recommended if the surgery is considered a high or intermediate risk and the patient has poor functional capacity. It can be of value in patients with one or more cardiac risk factors or those having clinical signs of cardiovascular disease. Routinely performing ECGs in all patients with obesity cannot be recommended.^[95]

Perioperative Implications of Weight Loss Medications

Weight loss medication can be prescribed to a patient suffering from obesity as part of a multimodal approach to management of the condition. The anesthesiologist must be aware of all the patient's current medications, including nonprescription appetite suppressants and diet supplements, some of which can have important side-effects and implications in the perioperative period. The anesthesia provider must be aware of potential interactions with the patient's other existing medications.

There are five commonly used weight loss medications in the United States: Phentermine, Phentermine/Topiramate, Orlistat, Lorcaserin, and Bupropion/Naltrexone. Familiarity with their mechanism of action and side-effect profile will facilitate appropriate risk–benefit decisions at the time of perioperative assessment (see Table 2). Of these

medications, only Orlistat has a peripheral mechanism of action. It is a gastric and pancreatic lipase inhibitor that reduces absorption of fat in the gut and thereby decreases caloric intake.^[97] The remainder of the medications all have more systemic effects based on their mechanisms of action and may influence the hemodynamic response during the perioperative and intraoperative anesthetic management.^[98]

The risk of serotonin syndrome should be considered with Lorcaserin and Bupropion/Naltrexone. The potential amphetamine-like effects of Phentermine/Topiramate should be acknowledged. The Bupropion/Naltrexone combination presents both possible challenges to traditional opioid-based perioperative pain management and the potential for opioid withdrawal.

Prior Weight Loss Surgeries and Implications for Subsequent Anesthesia

After a restrictive weight loss procedure, which includes gastric banding and sleeve gastrectomy, patients are at an increased risk of gastric reflux. These patients may benefit from anti-acid premedication and should be considered for rapid sequence induction.^[99,101]

Malabsorptive procedures, like Roux-en-Y gastric bypass or anastomosis gastric bypass, cause a loss of surface area which may affect oral medication absorption (e.g., postoperative oral opioid absorption).

Risk Assessment of the Obese Patient

There are numerous scoring systems used to assess perioperative risk. Some scoring systems are specific to the bariatric population. Examples are the Obesity Surgery Mortality Risk Score (OS-MRS) and the Edmonton Obesity Staging Systems (EOSS). Other scoring systems include the ASA Physical Status, the Revised Cardiac Risk Index (RCRA), the Physiological and Operative Severity Score for the Enumeration of Mortality and Morbidity (POSSUM), and the American College of Surgeons Surgical Risk Calculator, all of which serve as a general scoring system for the population as a whole.

The OS-MRS is a validated risk stratification score in patients undergoing gastric bypass surgery and is used to identify risk factors associated with mortality [Table 3].

The EOSS is another bariatric scoring system that can be used to help identify individuals at an increased risk of mortality.^[102] The EOSS categorizes patients with obesity into one of five

Table 2: Commonly used US FDA-approved drugs for weight management (D art)

Drug name	Mechanism of Action	Common Side Effects
Phentermine	Noradrenergic; generalized sympathetic activation	Elevated blood pressure and heart rate; dizziness, insomnia, headache, anxiety
Lorcaserin	Selective Serotonergic 5-HT2C receptor agonist	Dizziness, nausea, hypoglycemia, serotonin toxicity
Orlistat	Lipase inhibitor	Gastrointestinal symptoms, malabsorption of vitamins
Phentermine/ Topiramate	Noradrenergic and GABA receptor activator	Headache, dizziness, elevation in heart rate and blood pressure, dry mouth, memory changes
Bupropion/ Naltrexon	Bupropion inhibits the reuptake of norepinephrine and dopamine; it causes release of beta-endorphins, an endogenous agonist of mu-receptors; naltrexone effect on mu-receptors offers a synergistic effect to the desired one by Bupropion in this particular use	Nausea (most common adverse effect)

obesity stages by evaluating obesity related comorbidities and functional status [Table 4]. EOSS >2 correlates with a higher mortality; however, further validation will be necessary. EOSS 2, 3, and 4 were significantly associated with major complications. The strongest associations with major complications were EOSS 4 with an OR of 2.3 (2.11-2.51)^[103] Higher EOSS scores are independently associated with 30-day major postoperative complications and mortality.

According to the 2015 guidelines published by the Association of Anaesthetists of Great Britain and Ireland and the Society for Obesity and Bariatric Anaesthesia for perioperative management of the obese patient, a patient’s cardiovascular status should be assessed in the same way regardless of whether a patient has obesity or not. Efforts should be made to identify the presence of metabolic syndrome, however, as it is associated with cardiac morbidity. The decisions for specific cardiac investigations should be based on exercise tolerance, comorbidities, and the extent of surgery.^[73]

The search of a more precise assessment tool in identifying the bariatric patient’s risk after surgery is still ongoing. BMI, age, and duration of obesity needs to be considered, when developing a more precise tool in assessing the “burden” of obesity and its impact on postoperative complications.

Ambulatory versus Inpatient Surgery in Patients with Obesity

The decision to perform surgery on patients with obesity as inpatient or outpatient should be part of the preoperative assessment and should be tailored toward the individual patient, his/her comorbidities, the type of surgical procedure, its risk, and the choice of anesthetic technique.

Patients with a BMI >50 kg/m² are under increased risk of complications and may be poor candidates for ambulatory surgery,^[99] as they have an increased risk of requiring

Table 3: Obesity Surgery Mortality Risk Score (OS MRS)

Obesity Surgery Mortality Risk Score (OS-MRS)		
Risk Factor	Points	
BMI > 50 kg/m ²	1	
Male gender	1	
Age > 45	1	
Hypertension	1	
Risk factors for pulmonary thromboembolism (prior venous thromboembolism, vena cava filter, hypoventilation, pulmonary hypertension)	1	
Risk Group	Score	Postoperative mortality
Low risk	0-1	0.3
Moderate risk	2-3	1.7
High risk	4-5	3.2

overnight admission after general anesthesia, especially when combined with poor pain control.^[104]

In addition to BMI, other considerations make patients with obesity poor candidates for ambulatory surgery. These conditions include poorly controlled hypertension, ischemic heart disease, a history of congestive heart failure, advanced respiratory disease (i.e., untreated OSA/OHS or low preoperative oxygen saturation), the requirement for long-acting opioids for postoperative pain control, and metabolic syndrome. When using scoring systems, a patient with obesity who is an OS-MRS class 4-5 is a poor ambulatory surgery candidate.

Ideally, patients with OSA should have their surgery scheduled early in the day to allow for possible longer recovery and monitoring times.

Premedication and Perioperative Pharmacological Management of Patients with Obesity

Premedication is an important part of preoperative management of all patients coming for surgery. That involves the optimization of underlying medical conditions

Table 4: Edmonton Obesity Staging Systems (EOSS)

EOSS Score	Definition
0	No sign of obesity-related risk factors No physical symptoms No psychological symptoms No functional limitations
1	Patient has obesity-related subclinical risk factors (borderline hypertension, impaired fasting glucose, etc.) Mild physical symptoms (not requiring medical treatment for comorbidities) Mild obesity-related psychological symptoms (but quality of life not impacted)
2	Established obesity-related comorbidities requiring medical management (hypertension, type 2 diabetes, obstructive sleep apnea, polycystic ovarian syndrome, osteoarthritis, reflux disease) Moderate obesity-related psychological problems (depression, eating disorder, anxiety) Moderate functional limitations in daily activity
3	Significant obesity-related end-organ damage (myocardial infarction, heart failure, diabetic complications, incapacitation osteoarthritis) Significant obesity-related psychological symptoms (major depression, suicidal ideation) Significant functional limitations (unable to work or complete routine activities)
4	Severe obesity-related comorbidities Severely disabling psychological symptoms Severe functional limitations

*The score is based on the highest stage risk factor present in the patient (e.g., a patient who would, otherwise, fall into category 0 but has hypertension would therefore be a stage 2)

and implementation of risk reduction therapies. The most important aspect is thorough assessment of each patient and tailoring the premedication to their specific needs.^[100,105] The main aims of premedication are as follows:

- Optimization of patients' underlying medical conditions for surgery
- Risk-reduction therapies such as aspiration prophylaxis
- Anxiolysis
- Analgesia.

The physiologic changes associated with obesity alter the pharmacokinetics of most drugs. Morbid obesity impacts many organ systems decreasing the margin of safety of different drugs, including anesthetic medications. The factors affecting the pharmacodynamic and pharmacokinetic characteristics of anesthetic agents in morbid obesity are as follows:

- Increased cardiac output
- Increased lean body weight (LBW)
- Increased extracellular fluid volume
- Increased fat mass.

In normal-weight patients, drug dosing is usually individualized based on total body weight (TBW). However, in patients with obesity, adipose tissue and LBW do not

increase proportionally. While the fat weight increases proportionally to TBW, the percentage of LBW per kilogram of TBW decreases. In morbidly obese patients, cardiac output and LBW are important parameters to determine a medication dose. LBW is total body water minus body fat weight. There is a linear relationship between LBW and clearance for many drugs. LBW is an important parameter for maintenance dosing determination in obesity.^[25]

The major objectives of pre-anesthetic medication are to decrease the stress response, preserve hemodynamic parameters, facilitate anesthesia induction, and produce amnesia. Different medications may be used for premedication, including benzodiazepines, alpha-2 agonists, melatonin, and gabapentinoids.

Benzodiazepines

Midazolam

- Dose: for premedication, 150-350 mcg/kg IV injection over 20-30 seconds
- Oral midazolam (at a dose of 0.25 mg/kg) has shown sedative, anxiolytic, and anterograde amnesic effects with no adverse effects on hemodynamic stability or recovery in adults undergoing outpatient surgery under general anesthesia
- Onset: 15-20 min (PO)
- Protein bound: 97%
- Metabolized by liver via CYP3A4
- Metabolites: 1-hydroxymethylmidazolam
- Elimination half-life: 2-6 hours
- Excretion: urine (90%).

In patients with morbid obesity, systemic clearance of midazolam is unchanged, while oral bioavailability is increased. Oral benzodiazepines cause little or no respiratory depression and are suitable for preoperative anxiolysis in patients with obesity.^[106]

Midazolam is a commonly used lipophilic benzodiazepine for preoperative sedation because of its potent sedative, amnesic, and anxiolytic properties. Midazolam is metabolized to its major metabolite 1-OH-midazolam and rapidly excreted into the urine as its glucuronide conjugate. While it has previously been suggested that its clearance in patients with obesity is reduced as compared with non-obese patients, more recent studies on the pharmacokinetics of midazolam in obesity have shown no alteration in midazolam clearance as compared with adults without obesity.^[63,107]

The volume of distribution (Vd) of midazolam increases substantially with body weight, resulting in lower concentrations after intravenous bolus administration.^[108] Nevertheless, if intravenous midazolam is used in patients with obesity, they should be monitored and have supplemental oxygen available.^[63]

Greenblatt *et al.* found that the Vd of midazolam in subjects with obesity (Vd 114 liters, mean weight of 117 kg) greatly exceeded that measured in lean subjects (Vd 31 liters, mean weight of 66 kg).^[108] They concluded that the dose of midazolam should be increased in proportion to TBW. The clearance of midazolam in subjects with obesity tends to be slightly lower than in lean subjects. From a pharmacodynamic point of view, however, it must be realized that patients with obesity are often sleep-deprived and may be more sensitive to the effects of benzodiazepines.^[109]

Concomitant use of benzodiazepines, including midazolam, and opiates may result in profound sedation and respiratory depression.^[110]

Oral alprazolam has also been traditionally used as a premedication in patients with obesity.

Alpha-2 agonists

Alpha-2 agonists have shown favorable properties in bariatric patients.

Dexmedetomidine

Dexmedetomidine, an alpha-2 agonist, does not cause respiratory depression or contribute to upper-airway obstruction, which is attributed to its pharmacological properties. Dexmedetomidine acts on the locus coeruleus and causes an electroencephalography activity reading similar to natural sleep, unlike conventional GABA-aminergic sedatives.^[111] Dexmedetomidine also offers sufficient sympathetic blockade. Dexmedetomidine can be given intranasally to morbidly obese patients with a dosing recommendation of 1 mcg/kg of ideal body weight and has been shown to be a better premedication option than oral alprazolam.^[112] Clonidine has an elimination half-time four times that of dexmedetomidine and a correspondingly longer duration of effect. However, in common with dexmedetomidine and ketamine, it can be used as an adjunct to reduce dosage requirements for analgesics and sedatives. In patients with OSA, oral clonidine premedication, in a dose of 2 mcg/kg, has been shown to stabilize hemodynamic variables during induction, maintenance, and emergence from anesthesia and to reduce the need of intraoperative anesthetics and postoperative opioids without deterioration of ventilation.^[113]

Melatonin

Melatonin is a hormone produced by the pineal gland and regulates sleep cycle. Melatonin may be particularly useful when traditional hypnotics are contraindicated.

A systematic review provides compelling evidence that melatonin premedication is effective in ameliorating perioperative anxiety in adults. The analgesic effects of melatonin in the adult population during the perioperative period is controversial.^[114]

Melatonin has sedative, analgesic, and hypnotic properties and is an effective premedication for reducing stress and anxiety in obese patients, prior to anesthesia and surgery. Due to its unique properties, it may also improve sleep quality and recovery from surgery and anesthesia. The recommended premedication dose of melatonin in adults is 3 to 5 mg.

A systematic review of pharmacokinetic studies in adult patients and volunteers revealed the bioavailability of orally dosed melatonin to be approximately 15% (range 9–33%) and time to maximum plasma concentration (C_{max}) was about 50 minutes for an immediate-release formulation. Study designs and analysis methods varied extensively; however, other factors that may impact the kinetics of melatonin include age, caffeine, smoking, and oral contraceptive use.^[115]

Melatonin has mild and relatively few side-effects, such as drowsiness, headache, and gastrointestinal disturbances.^[116]

Gabapentinoids

Pregabalin

- Bioavailability: >90%
- Peak plasma time, fasting: 1.5 hour (oral)
- Protein bound: none
- Elimination half-life: 6.3 hours
- Excretion: urine.

Oral pregabalin, given preoperatively, in a dose of 300 mg has been shown to alleviate patients' pain and reduce nausea and vomiting after laparoscopic gastric bypass surgery without any side-effects.^[117] The use of preoperative pregabalin has been shown to significantly reduce opioid requirements within the first 24 hours postoperatively.^[118]

Gabapentin

- Bioavailability: 27-60%
- Peak plasma time, fasting: 2 to 3 hours (oral)
- Protein bound: none

- Elimination half-life: 5 to 7 hours
- Excretion: urine.

Gabapentin is less potent than Pregabalin. It has nonlinear pharmacokinetic, as compared to the linear one of Pregabalin. It has a highly variable bioavailability. Respiratory depression has been described when used with opioids. Sedation is a known side-effect when administered in conjunction with benzodiazepines. The perioperative use of gabapentinoids to reduce opioid consumption must be balanced against the risk of adverse effects such as dizziness and increased sedation.^[119]

Conclusion

Managing the patient suffering from obesity continues to be a challenging task for the anesthesia providers. Delivering safe care to this high-risk population begins with thorough and proactive anesthesia assessment, preoperative preparation, and optimization. Better understanding of the different types of obesity, underlying pathophysiology, identification of clinically relevant biomarkers, and risk stratification is required and remains the focus of the current obesity research. The anesthesia management needs to be tailored to the specific patient's physiological changes. The anesthesia administration in obesity may be better served by the creation of a specialized anesthesia team and a structured, multidisciplinary approach to preparation and postsurgical management of the super-obese. Planning early in the patient preoperative course for possible postoperative requirements is essential and should be encouraged in this population.

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Conflicts of interest

There are no conflicts of interest.

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