INTRODUCTION AND DEFINITIONS

Obesity has become one of the most important public health problems confronting industrialized nations. In 1997 the prevalence of obesity in Europe was 15%-20%. The situation in the USA was even worse. The concept of ideal body weight (IBW) originates from life insurance studies which describe the weight associated with the lowest mortality rate for a given height and gender. IBW can be estimated from the formula IBW (kg) = height (cm) – x, where x is 100 for adult males and 105 for adult females. Obesity can be defined as more than 20% above IBW and morbid obesity as more than twice IBW. The body mass index (BMI) is a more robust measure of the relationship between height and weight and is widely used in clinical and epidemiological studies: BMI = body weight (kg)/height² (m). A BMI < 25 kg/m² is considered normal, a person with a BMI of 25-30 kg/m² is considered overweight but at low risk of serious medical complications while those with a BMI > 30, > 35 and > 55 kg/m² are considered obese, morbidly obese and super-morbidly obese respectively. Morbidity and mortality rise sharply when the BMI is > 30 kg/m².

Obesity is associated with many chronic health problems such as cardiovascular disease, diabetes mellitus, arthritis and cancer.

Given recent reports that bariatric surgery offers sustained reductions in body weight, it is certain that anesthesiologists are going to care for an increasing number of obese patients in the foreseeable future. These patients may present a considerable challenge because of the pathophysiology and complications associated with obesity.

Bariatric operations can be broadly categorized by their mechanism of either restricting food intake or inducing maldigestion/malabsorption. The most frequently performed procedures are the laparoscopic adjustable gastric band and the Roux-en-y gastric bypass.

The laparoscopic adjustable gastric band (LAGB) consists of two components, a silicone band with an inner inflatable cuff and a reservoir connected by tubing. The band is placed around the gastric cardia to create a small proximal gastric pouch with an adjustable restrictive outlet that limits the amount of food that can be consumed. Advantages of this technique are the very low operative morbidity and mortality. Disadvantages are its apparent inferior outcomes regarding weight loss and the substantial intermediate and long-term complications with reports of band slippage, gastric perforation, band erosion and malfunction requiring reoperation in up to 20% of patients.

Roux-en-y gastric bypass combines the restrictive effect of a small proximal cardia pouch and the maldigestive effect of a 75- to 150-cm Roux limb. Advantages include established long-term effectiveness for sustained weight loss, reduction of comorbidities and minimal risk for long-term nutritional sequelae.
PATHOPHYSIOLOGIC CHANGES IN OBESITY AND ANESTHETIC PROBLEMS

Respiratory system

It is well established that obesity is associated with hypoxemia and this through several mechanisms, increased minute ventilation requirement at rest to meet the metabolic needs of increased tissue mass, increased work and energy cost of breathing and changes in lung volumes. Changes in lung volumes at rest manifest as reduced functional residual capacity (FRC), vital capacity and total lung capacity. These reductions in lung volumes increase exponentially with increasing BMI. Reduced FRC can result in lung volumes below closing capacity in normal tidal ventilation. Ventilation-perfusion mismatches develop from the closure of small airways resulting in right-to-left shunt and arterial hypoxemia.

Anesthesia compounds these problems with a greater reduction in FRC in obese patients compared with non-obese patients. This reduction in FRC also leads to reduced capacity of obese individuals to tolerate periods of apnea.

Patient positioning can aggravate these lung volumes. Boyce et al. have shown a significant extension of the safe apnea period in these patients by employing the 30° reverse Trendelenburg position during induction of anesthesia.

Not surprisingly, obese patients suffer from a greater percentage of postoperative atelectasis for a longer period of time after a general anesthetic.

A special subset of patients are the obese patients with sleep apnea.

Obesity and obstructive sleep apnea syndrome (OSA)

Osa is defined as a cessation of airflow for more than 10 seconds despite continuing ventilatory effort, five or more times per hour of sleep, and is usually associated with a decrease in arterial oxygen saturation of more than 4%. The incidence of OSA is 2% in women and 4% in men, 60% to 90% of patients with OSA are obese.

OSA repeatedly disrupts sleep due to increased ventilatory effort-induced arousal which in turn causes daytime sleepiness and altered cardiopulmonary function.

Obesity causes OSA because of the inverse relationship between obesity and pharyngeal area due to the deposition of adipose tissue into pharyngeal tissues. This increases the likelihood that relaxation of the upper airway muscles will cause collapse of the soft-walled pharynx between uvula and epiglottis. Deposition of fat not only narrows the airway but also changes the shape of the pharynx.

The upper airway in obese patients is also compressed externally by superficially located fat masses. The neck is significantly fatter in obese OSA patients compared to equally obese non-OSA patients and the incidence and severity of OSA correlates better with increased neck circumference than with general obesity.

Over the course of an apnea a number of important respiratory events occur which will ultimately result in serious systemic pathophysiologic consequences.

Decreases in PaO2 may cause bradycardia. In half of the OSA patients long sinus pauses, second-degree heart block and ventricular dysrhythmias occur. This high incidence of arrhythmias may explain the higher incidence of nocturnal angina and myocardial infarction in these patients.

Pulmonary hypertension is a result of the hypoxic pulmonary vasoconstriction, the negative intrathoracic pressure with increasing ventilatory effort and the decrease in PaO2.

Arterial hypertension is caused by the innumerable repetitive increases in sympathetic tone that occur with each hypoxemic-hypercapnic arousal event.

Pulmonary and arterial hypertension account for the 70% and 30% incidence of right and left ventricular hypertrophy.
The many brief periods of sleep diminish restorative deep sleep. This causes daytime sleepiness and fatigue, morning headaches, diaphoresis, nocturnal enuresis, decreased cognition and intellectual function and personality and behavioral changes.

A presumptive clinical diagnosis of OSA can be made in a patient with the classical signs and symptoms of obesity, snoring and apnea during sleep, apparent arousal and daytime sleepiness or fatigue. Since a diagnosis of OSA will impact on anesthetic management, all obese patients should be routinely asked about these symptoms. It may be prudent to postpone the surgery and refer the patient to an appropriate physician. The definitive diagnosis must be made by some form of sleep study.

An increased risk for postextubation complications has been reported in adult obese patients with OSA, and many of these patients may be particularly sensitive to opioid and sedative medications.

**Obesity and difficult intubation?**

The overall incidence of difficult intubation is reported to be 5.8%. Juvin et al. reported an incidence of 2.2% in 134 normal weight patients and an incidence of 15.5% in 129 patients with a BMI > 35 kg/m². The study performed by Shiga et al. in 2005 resulted in a 15.8% difficult intubations in obese patients. In contrast to these results Brodsky et al. found only a 3% incidence of difficult intubation in patients with a BMI > 40 kg/m² and no association between increasing BMI and problematic intubation. The 38 difficult intubations in 461 patients in the study by Karkouti et al. were not associated with height, weight nor BMI.

What can be the reason for these conflicting results?

A first possible reason could be the bad positioning of obese patients. The standard sniffing position for tracheal intubation is achieved in non-obese patients by raising the occiput 8 to 10 cm with a pillow or head rest. Obese patients require much greater elevation of their head, neck and shoulders to produce the same alignment of axes for intubation. Elevating the upper body and head of morbidly obese patients to align their sternum and ear in a horizontal line results in a significant improvement in laryngoscopic view.
A second reason appears to be that most studies don’t differentiate between difficult laryngoscopy and difficult intubation.

One thing that can be concluded is that the standard clinical tests for predicting difficult intubation are not useful among morbidly obese patients. Juvin concluded that the only independent risk factor for difficult intubation was a Mallampati 3-4, but with a low specificity, sensitivity and negative predictive value in obese patients. Brodsky stated that the best predictor of problematic intubation is neck circumference (measured at the superior border of the cricothyroid cartilage). With a neck circumference of 40 cm there’s a 5% probability of a difficult intubation, with a neck circumference of 60 cm this is 35%. Difficult intubation and OSA have been found to be significantly related.

The decision as to whether perform an awake intubation must be individualised on the basis of a complete preoperative airway evaluation. Proper preparation should depend on thorough topical and nerve block anesthesia of the upper airway. If intubation is to be done with the patient asleep, “cannot intubate, cannot ventilate” options must be immediately available. Desaturation develops more rapidly in obese patients despite preoxygenation, due to a reduction in FRC.

Depending on the ease of mask ventilation and tracheal intubation at the beginning of the case, the length and type of surgery and the presence and severity of OSA, one should consider leaving the patient intubated for a period of postoperative mechanical ventilation. The patient is extubated when he is fully awake. Full recovery of neuromuscular block should be proven and the patient is extubated in semi-upright position.

If the patient was on CPAP preoperatively, he should be on CPAP postoperatively.

**Cardiovascular pathophysiology**

Cardiovascular disease dominates the morbidity and mortality in obesity and manifests itself in the form of hypertension, ischaemic heart disease and cardiac failure.

**Hypertension**

Mild to moderate hypertension is seen in 50%-60% of obese patients and severe hypertension in 5%-10%. An expansion of the extracellular volume, resulting in hypervolemia and an increase in cardiac output are characteristic of obesity-induced hypertension. Hyperinsulinemia, which is characteristic of obesity, can contribute by activating the sympathetic nervous system and by causing sodium retention. Insulin resistance may be responsible for the enhancement in pressor activity of norepinephrine and angiotensin 2.

Hypertension leads to concentric left ventricular hypertrophy and a progressively non-compliant left ventricle, which, when added to the increased blood volume, increases the risk of cardiac failure.

**Ischaemic heart disease**

It is now generally accepted that obesity is an independent risk factor for ischaemic heart disease. Other factors such as hypertension, diabetes mellitus, hypercholesterolaemia and reduced high density lipoprotein levels, which are all common in the obese, will compound the problem.

**Cardiac function**

The morbidly obese individual is at risk of a specific form of obesity-induced cardiac dysfunction, although the belief that this is secondary to fatty infiltration of the heart is no longer valid. Obesity is associated with an increase in blood volume and cardiac output. This increased cardiac output is largely a result of ventricular dilation and an increase in stroke volume. The ventricular dilation results in increased left ventricular wall stress leading to hypertrophy. Such eccentric left ventricular hypertrophy results in reduced compliance and left ventricular dysfunction, i.e. impairment of left ventricular filling, leading to elevated left ventricular end-diastolic pressure and pulmonary oedema.

The capacity of the dilated ventricle to hypertrophy is limited. So when left ventricular wall thickening fails to keep pace with dilation, systolic dysfunction ensues, the obesity cardiomyopathy. Ventricular hypertrophy and dysfunction worsen with increasing duration of obesity and improve to some extent with weight loss.

Morbidly obese subjects often have very limited mobility and may therefore appear asymptomatic even when they have significant cardiovascular disease. Many individuals prefer to sleep upright and therefore deny the symptoms of orthopnea and paroxysmal nocturnal dyspnea. Asking the patient to walk the length of the ward may reveal a markedly reduced exercise tolerance, and assuming the supine position may produce significant orthopnea and even cardiac arrest.

The obese patient should have a detailed and thorough cardiovascular examination, looking in particular for evidence of hypertension and cardiac failure.
**Pharmacokinetic implications of obesity**

The physiological changes produced by obesity can markedly affect the distribution, binding and elimination of anesthetic drugs. Systematic knowledge regarding these effects is lacking. Most drug-dosing guidelines are based on results from relatively small studies in moderately obese patients.

Obesity increases both fat and lean masses. The increase in lean body mass represents 20% to 40% of total excess of weight. These changes in tissue distribution can markedly affect the volume of distribution of anesthetic drugs. Highly lipophilic substances show significant increases in volume of distribution.

The effects of obesity on drug binding to the plasma proteins are still unclear. The increased concentration of triglycerides, lipoproteins, cholesterol and free-fatty acids may inhibit protein binding of some drugs, increasing their free plasma concentrations. On the other hand, the increase in concentrations of acute phase proteins may also increase the degree of binding of other drugs, reducing their free plasma concentrations.

Changes in elimination can result from obesity-induced changes of liver or kidney function. The fatty degeneration of the liver may progress to liver fibrosis and affect hepatic clearance. Renal clearance increases because of the increase in kidney weight, renal blood flow and glomerular filtration rate.

Drugs whose distribution is restricted to lean tissues should be dosed based on ideal body weight (IBW) for the loading dose. For those drugs which distribute freely into adipose tissue, the loading dose should be based on total body weight (TBW). Maintenance doses depend on clearance rates.

Dosing guidelines for the drugs most frequently used during anesthesia cannot easily be distilled from the literature, because different sources give different numbers.

### Induction agents

Thiopental is a highly lipophilic substance and has a larger volume of distribution in obese patients and a longer elimination half-life. Obese patients appear to be more sensitive and should receive a dose based on LBM. **BUCKLEY et al.** however suggested a higher dose because of the elevated cardiac output found in the obese, resulting in a lower peak plasma concentration.

The volume of distribution and clearance of propofol correlate with TBW. Elimination half-life is similar in obese and lean patients without signs of propofol accumulation. The dose regimen for both induction and maintenance of anesthesia should be based on TBW. However the cardiovascular effects of very large doses of propofol remain uncertain especially considering the physiological changes induced by obesity on cardiovascular homeostasis. It seems prudent to carefully titrate propofol administration based on LBM or to use a corrected weight (IBW + 40% excess weight). Igarashi and colleagues however reported two cases of intraoperative awareness during propofol anesthesia when using the Diprifusor device with adjusted body weight.

<table>
<thead>
<tr>
<th>Agent</th>
<th>Weight</th>
<th>Dosing</th>
</tr>
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<tbody>
<tr>
<td>Propofol</td>
<td>Induction : LBW, maintenance : TBW</td>
<td>Systemic clearance and $V_d$ at steady-state correlates with TBW. High affinity for excess fat. High hepatic extraction and conjugation relates to TBW. Cardiovascular depression – limits dosage</td>
</tr>
<tr>
<td>Thiopental</td>
<td>Induction : LBW</td>
<td>Increased $V_d$, increased blood volume, cardiac output, and muscle mass means increased absolute dose. Increased elimination half-life. Cardiovascular depression – limits dosage</td>
</tr>
<tr>
<td>Succinylcholine</td>
<td>TBW</td>
<td>Plasma cholinesterase activity increases with TBW</td>
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<tr>
<td>Vecuronium</td>
<td>IBW</td>
<td>Recovery is delayed if given according to TBW</td>
</tr>
<tr>
<td>Rocuronium</td>
<td>IBW</td>
<td>Recovery is delayed if given according to TBW</td>
</tr>
<tr>
<td>Atracurium</td>
<td>IBW</td>
<td>Prolonged duration of action on obese patients has been demonstrated even if dose is based on IBW</td>
</tr>
<tr>
<td>Cis-atracurium</td>
<td>IBW</td>
<td>Titrate to effect. Dosing based on TBW may cause overdosing</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>LBW</td>
<td>Titrate to effect. Dosing based on TBW may cause overdosing</td>
</tr>
<tr>
<td>Sufentanil</td>
<td>LBW</td>
<td>Titrate to effect. Dosing based on TBW may cause hypotension and bradycardia</td>
</tr>
<tr>
<td>Remifentanil</td>
<td>LBW</td>
<td>Titrate to effect. Dosing based on TBW may cause hypotension and bradycardia</td>
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Benzodiazepines

Benzodiazepines are highly lipophilic drugs, distribution volume and elimination half life increase in parallel with body weight. When using a single intravenous bolus the dose should be increased in proportion to TBW. In a continuous infusion the dose should be adjusted to IBW, because total clearance is not substantially changed compared with lean subjects.

Muscle relaxants

Muscle relaxants are polar and hydrophilic drugs and are distributed to a limited extent in excess body fat.

VARIN et al. evaluated the pharmacokinetics and pharmacodynamics of atracurium in obese and lean patients and found no differences in volume of distribution, elimination half-life and total clearance. They observed no difference in time of recovery from neuromuscular blockade and recommended a dose based on TBW. KIRKEGAARD-NIELSEN et al. however observed a prolonged duration of action in obese patients, even with a dose based on IBW. They suggested that the atracurium dose be reduced for each kg above 70 kg.

Vecuronium should be dosed based on IBW in obese patients.

PUHRINGER et al. found no differences in plasma clearance, distribution and elimination half life of rocuroniumbromide, indicating that pharmacokinetics and pharmacodynamics were not altered by obesity. LEYKIN et al. however observed a more than doubling in duration of action when rocuronium dosage was based on TBW compared to IBW in obese patients. The differences in the results of these two studies could be caused by the fact that the patients in the Puhringer study were only moderately obese (BMI > 30), while they were morbidly obese (BMI > 40) in the second group.

Duration of action of succinylcholine is primarily determined by the level of pseudocholinesterase activity. BENTLEY et al. reported that increasing weight is associated with increased pseudocholinesterase activity. Succinylcholine should be administered on the basis of TBW.

Opoids

All synthetic opioids are highly lipophilic drugs. No definite conclusions can be made from the limited studies, but the findings suggest that dose regimens for fentanyl, sufentanil and alfentanil be based on LBM rather than actual weight.

Remifentanil is susceptible to hydrolysis by blood and tissue esterases resulting in rapid metabolism to essentially inactive products. A study by EGAN et al. evaluated the pharmacokinetics of remifentanil in obese and lean patients. The volumes of distribution were less than expected for lipid-soluble molecules and revealed only modest distribution into body tissues, with no differences between obese and lean patients. The clearance of remifentanil was similar in the two groups. Remifentanil pharmacokinetics appear to be more closely related to LBM than TBW.

Intravenous administration of any opioid should be carefully titrated according to individual patient needs.

Volatile anesthetics

Obese patients are traditionally reported to have a slower emergence from anesthesia because of a delayed release of volatile drugs from the excess fat tissue. Desflurane and sevoflurane have much lower lipid solubility and have each been suggested as the volatile anesthetic of choice for obese patients because of their rapid and consistent recovery profile.

Is one of these two volatile anesthetics superior to the other for use in the obese population? STRUM et al. reported a faster recovery with desflurane compared to sevoflurane, while ARAIN et al., on the other hand, found no differences in emergence and recovery profile. They explained these results because of their careful titration of anesthetic depth with the help of BIS-monitoring. There are some reports of significantly higher fluoride serum concentrations after sevoflurane anesthesia in obese than in non-obese patients. Other researchers did not find significant differences in fluoride serum concentrations and no signs of renal dysfunction have been demonstrated.

Local anesthetics

Fatty infiltration of the epidural space, as well as increased blood volume caused by the increased intra-abdominal pressure, may reduce the volume of the epidural space, resulting in an unpredictable spread of the anesthetic solution and block height.

Obesity and gastrointestinal disorders

Based on early research by VAUGHAN et al. obesity alone has long been considered as a risk factor for aspiration of gastric contents during
induction of anesthesia. For obese patients undergoing elective interventions, this concept has recently been challenged. Gastric emptying of solids in obese subjects is faster, slower or no different from non-obese patients, according to the different studies. Although the actual incidence of clinically significant aspiration in this population is difficult to determine, and it is probably quite low, management of a difficult airway contributes to its occurrence. Positioning obese patients in 45° or 30° reverse Trendelenburg may aid in the prevention of gastrooesophageal reflux and, thus, aspiration by alleviating increased intra-abdominal pressure.

POSTOPERATIVE PAIN MANAGEMENT

Most commonly used strategies employ either patient-controlled intravenous analgesia (PCA) or thoracic epidural analgesia (TEA). Surgical technique (open versus laparoscopic) may influence the patients and anesthesiologists choice of pain treatment. Either strategy may offer specific advantages for specific patient outcomes, such as reduced rate of pulmonary complications after abdominal surgery and superior pain control with TEA or less impairment to ambulate with PCA. The initial PCA setting should be based on estimated lean body mass and there should be no continuous opioid background infusion.

CONCLUSION

A thorough understanding of the pathophysiology and specific implications of obesity should allow more effective and safer treatment for this unique group of patients. Outcome data on anesthetic care and perioperative pain management in bariatric surgery patients are scarce. Possible areas for future research include studies on patient safety and outcome, pharmacokinetic and pharmacodynamic studies of anesthetics, analgesics and other perioperative medications, studies of reduced-opioid or non-opioid based pain management strategies, studies on the impact of sleep-disordered breathing syndromes (e.g. OSA) and development of accurate and well-tolerated physiological monitoring devices for severely obese patients, particularly for blood pressure assessment.

References

8. A report by the American society of anesthesiologists task force on perioperative management of patients with obstructive sleep apnea, Practice guidelines for the perioperative management of patients with obstructive sleep apnea, Anesthesiology, 104, 1081-1093, 2006.