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Abstract

Patients with morbid obesity are a growing patient population. These patients present a unique set of challenges in healthcare management. These unique challenges have been a long-standing concern to anesthesia providers in appropriately managing postoperative pain with opioids. Multimodal analgesia strategies have been adopted by many providers to minimize opioid-related side effects that are highly desirable in bariatric surgical procedures. The literature reviewed for this manuscript highlights the challenges this population presents to anesthesia providers, as well as conclusively supports alternative approaches utilizing multimodal pain management.
Perioperative Pain Management in Morbidly Obese Patients Undergoing Bariatric Surgery

Obesity has been an increasing epidemic in the United States for decades (CDC, 2022). According to the Centers for Disease Control (CDC; 2022), 42.4% of Americans classify as obese. Patients with severe obesity are more likely to experience chronic pain because of the increased pressure on their joints brought on by excessive weight (Heinberg et al., 2019). A similar increasing trend has been the number of prescription opioids in this country. Prescription opioid use has increased significantly over the years to help patients cope with acute pain from surgery and chronic pain (CDC, 2022). Opioids provide analgesia as well as euphoria, a combination that may lead many patients to continue opioid use after their surgery in order to cope with their chronic pain (CDC, 2022). The increase in opioid prescriptions for treating chronic pain has led to what the CDC and the Department of Health and Human Services have called an “epidemic” (Heinberg et al., 2019). A large-scale survey of over one million U.S. residents demonstrated a linear relationship between Body Mass Index (BMI) and chronic pain diagnoses (Heinberg et al., 2019). Compared to individuals with normal BMIs, overweight individuals reported 20% greater rates of chronic pain, and those considered morbidly obese reported 254% greater rates of chronic pain (Heinberg et al., 2019). The linear relationship between chronic pain and BMI has led many to conclude that opioid use leads to physical dependence among obese patients (Heinberg et al., 2019).

Aside from treating chronic pain, anesthesia providers are also faced with many other challenges with the obese population in the form of financial burdens imposed on hospitals and surgical risks to the patient. Medical costs for obese adults were $1,861 higher than those with a normal BMI (CDC, 2022). Opioids may play a role in these costs. Opioids increase surgical risks
through their adverse side effects, such as respiratory depression and post-operative nausea and vomiting (PONV). Opioids contribute to burgeoning hospital costs through increased length of stay due to suppressing gastric motility and immune responses. Because of both patient and hospital effects, many clinicians have sought to reduce their opioid prescriptions in favor of pain alternatives. As more research outlines the benefits of this field, many clinicians have sought an opioid-free anesthetic. An opioid-free anesthetic includes using anesthetic adjuncts such as the following: dexmedetomidine, non steroidal anti-inflammatory drugs (NSAIDs), acetaminophen, or ketamine to treat pain instead of opioids; this technique may provide patients with the pain relief needed while reducing the adverse side effects of opioids (Heinberg et al., 2019). This paper explores the research of treating morbidly obese patients undergoing bariatric surgeries to explain the demographic, the surgical risks associated, and how opioids exacerbate these risks while highlighting alternatives to reduce opioids intraoperatively.

**Background**

**Morbid Obesity**

To be defined as morbidly obese, an individual must meet one of the following requirements: have a body mass index (BMI) of 40 or more, be one hundred pounds over their ideal body weight, or have a BMI of 35 or greater combined with obesity-related health conditions, such as hypertension or diabetes (Stone et al., 2017).

Morbid obesity can cause post-operative complications, such as the exacerbation of chronic pain caused by increased stress on joints. Chronic pain only compounds the efforts of many clinicians to manage typical acute post-operative pain. Pain is often the cause for many to seek bariatric surgery, as weight reduction minimizes joint pain. Due to the prevalence of obesity, the frequency of bariatric surgery has been increasing worldwide. The prolific rise in
bariatric surgery has yielded many obese patients to reduce their weight to hopefully reduce their chronic pain. The anesthesia community's challenge is treating this pain intra-operatively without increasing risks to the patient (Stone et al., 2017).

**Cardiac Risks**

Obesity increases the risk of cardiovascular disease. Increased body mass increases metabolic demand, leading to an increase in cardiac output due to the increased blood volume necessary to sustain the fatty tissue, placing this population at higher risk for heart failure. Almost one-third of morbidly obese patients develop structural and functional changes as compensation for increased stroke volume (Sharma & Arora, 2020). These physiological changes can present as left ventricular dilation, which will eventually cause subsequent left-sided heart failure. Additionally, left atrial and ventricular enlargement heart remodeling can occur, which leads to an increased risk of nodal dysfunction, leading to atrial fibrillation or a prolonged QT interval. Both arrhythmias increase the risk of sudden cardiac death (Sharma & Arora, 2020).

Furthermore, a substantial increase in adipose tissue contributes to the release of bioactive mediators that promote a clinical inflammatory state that potentiates cardiovascular disease risks (Sharma & Arora, 2020). The metabolic syndrome resulting from obesity produces further disease progression in the form of insulin resistance, sodium retention, and sympathetic nervous system activation, in conjunction with the activation of the renin-angiotensin-aldosterone system. These mediators only compound hypertension, type 2 diabetes, and hyperlipidemia. The metabolic stress from cardiovascular disease also increases the risk of renal failure. Compounding the risks of renal failure, renal blood flow and GFR increase by 40%, secondary to the increased cardiac output and MAP in the obese population. Prolonged obesity
contributes to impaired nephron function, increasing arterial blood pressure and straining the heart further (Sharma & Arora, 2020).

**Vascular Risks**

Obesity also contributes to elevated clotting factors resulting in a chronic hypercoagulability state, leading to vascular disorders such as deep vein thrombosis (DVT) and pulmonary embolism (PE). The metabolic stress from cardiovascular disease also increases the risk of renal failure. Deep vein thrombosis and PE are the second leading cause of postoperative death after bariatric surgery, with an incidence of 2%. Development of a DVT or PE may be slow and can range from a few days after surgery to several months post-operatively (Kassir et al., 2016).

**Pulmonary Risks**

These patients may have an accumulation of adipose tissue on their thorax and abdomen, presenting an inverse relationship to respiratory function, which causes a restrictive airway by decreasing chest wall and lung compliance. Decreased pulmonary compliance leads to decreased functional residual capacity (FRC). As FRC decreases, a ventilation/perfusion (V/Q) mismatch arises, resulting in increased carbon dioxide (CO₂) retention, causing hypercarbia. Hypercarbia forces obese patients to take slower and shallower breaths, increasing their overall work of breathing to compensate for the increased physiological dead space (Sharma & Arora, 2020).

Inherently, obesity leads to other respiratory issues, such as obstructive sleep apnea syndrome (OSAS). The added redundant soft tissue in the oropharynx gives rise to a narrowed airway that can easily obstruct (Lam & Mui, 2016). Obstructive sleep apnea (OSA) affects 40-90% of the obese population. It stems from hypoxemia and hypercarbia that can set off a chain of events, such as pulmonary hypertension leading to heart failure. Severely obese patients may
develop obesity hypoventilation syndrome (OHS), whereby increased airway resistance from reduced lung volume can lead to alveolar collapse (\( \text{Pa CO}_2 > 45 \text{ mm Hg} \)). General anesthesia and the respiratory depressive effects of opioids used to treat pain only exacerbate the obstruction associated with obesity (Sharma & Arora, 2020).

**Bariatric Surgery**

The increased prevalence of obesity and comorbidities associated with the morbidly obese population has increased the number of bariatric surgeries performed. Bariatric surgery is associated with improved quality of life, decreased comorbidities, and improved survival in this population (Lee et al., 2016). In 2018, bariatric surgeries accounted for more than 250,000 surgeries performed in the United States, according to the American Society for Metabolic and Bariatric Surgery (Long-term Study of Bariatric Surgery for Obesity: LABS, 2022).

Laparoscopic bariatric surgeries are done more often because they are less invasive and safer than open bariatric surgery (Long-term Study of Bariatric Surgery for Obesity: LABS, 2022). The three most common bariatric surgery procedures include Roux-en-Y gastric bypass (RYGB), laparoscopic adjustable gastric band (LAGB), and sleeve gastrectomy (SG) (Lee et al., 2016). A RYGB involves constructing a small proximal portion of the stomach and attaches it directly to the small intestine. A LAGB involves inflatable bands placed around the proximal portion of the stomach to create a small pouch. Nothing is removed during this procedure, which makes it reversible. A SG involves the removal of a large portion of the stomach but no bypass (Lee et al., 2016). A visual depiction of different bariatric surgeries is available below (Figure 1).
Surgical Risks

Peritonitis is the most common complication after bariatric surgery due to anastomotic fistula formation. Peritonitis involves the inflammation of the thin layer of tissue in the abdomen, known as the peritoneum. Peritonitis is treated with antibiotics or with surgical intervention. Early complications of peritonitis occur within the first 10 days post-operatively and has an incidence of 1-6% in RYGB and 3-7% in SG. (Kassir et al., 2016).

Deep vein thrombosis and pulmonary embolism are the second leading cause of post-operative death after gastric surgery, with an incidence of 2% and a mortality rate of 20-30%. The risk increases in patients with a history of venous thrombosis. It may develop a few days post-operatively and persist for several months (Kassir et al., 2016).
Additionally, gastric ulcers occur in approximately 15% of patients after undergoing bypass surgery without a clearly established cause. Ulcers may develop during the first 90 days after surgery, and can be characterized by severe dysphagia, retro-sternal pain, and vomiting. Typically, ulcers are treated medically with proton pump inhibitors for 3 months.

Administering NSAIDs to patients for post-operative analgesia increases the risk of ulcers at the anastomosis site. NSAIDs block prostaglandin production, leaving the stomach lining vulnerable to its acid. Additionally, NSAIDs are already acidic, further irritating the stomach lining. As a result, long-term use (>30 days) increases the risk of ulcers and bleeding (Kassir et al., 2016).

Pain Management

Post-operative pain is common following bariatric surgery, particularly with laparoscopic bariatric surgeries (Okut et al., 2022). Thus, pain management after abdominal procedures is an integral component of post-operative care. Improper control can be associated with delayed ambulation and recovery, higher rate of complications, prolonged opioid usage, and higher health care costs with lower quality of life in this patient population. There are three components responsible for pain following laparoscopic surgery: parietal pain due to abdominal wall damage during trocar insertion, visceral pain due to irritation of the gastrointestinal serosa, and pain in the left shoulder caused by pneumoperitoneum irritating the diaphragm muscles (Okut et al., 2022). After laparoscopic surgery, parietal pain accounts for 50-70% of the pain reported by patients, visceral pain 10-20%, and 20-30% is pain from the pneumoperitoneum (Okut et al., 2022).

Opioids are typically utilized to provide pain relief. The United States, which contributes to only 4.4% of the world's population, consumes 80% of the world's supply of opioids (Stone et
Opioids are a typical analgesic administered throughout the perioperative period, but they have a variety of side effects that include respiratory depression, constipation, urinary retention, and at times dependence. Extensive retrospective studies reviewed by Stone et al. (2017) observed that many opioid naïve patients that underwent minor surgeries continued their opioid usage even a year after their surgery. Typical bariatric post-operative acute pain is expected for several weeks after surgery; however, after a year of managing 'post-operative pain,' it is questionable if the actual pain has a true organic cause or has been replaced by dependence (Stone et al., 2017).

**Opioids**

The mu (μ) receptor opioid agonists, such as morphine and fentanyl, are common opioids used for treating severe pain. The dorsal horn of the spinal cord is involved in pain transmission and, as such, is a significant site for the analgesic effects of opioids. Activation of μ receptors by opioid agonists inhibits the firing of C-fibers found in the primary afferent pathway on the dorsal horn in response to pain. Additionally, μ-opioid receptor agonists profoundly affect the high voltage-gated calcium channels located at the presynaptic terminals. They are primary sensory neurons in the dorsal root ganglion (Zeeni et al., 2019).

**Respiratory Depression**

The primary drive to breathe derives from central chemoreceptors in the brain (Palkovic et al., 2020). In the awake state, the cortico-limbic system of the forebrain influences respiration and respiratory activity, which changes with the level of physical activity, emotions, and arousal. When the "awake drive" is lost during sleep, there is a decrease in respiratory rate and a reduced hypoxic ventilatory response  (Palkovic et al., 2020).
Respiratory rate originates in the ventrolateral medulla, part of the brain stem. The inspiratory neuronal network activates the preBötzinger Complex to generate inspiration, and the expiratory neurons activate the Bötzinger Complex to generate expiration. A significant component of the chemodrive is routed through the Parabrachial Nucleus/Köllicker-Fuse Complex, causing phase-switching neurons in the preBötzinger Complex to activate inspiratory and expiratory motor neurons (Palkovic et al., 2020). Inhibitory inputs control the level of neuronal excitability in the preBötzinger Complex inspiratory neurons. Inputs from the preBötzinger Complex activate inspiratory and expiratory premotor and motoneurons (Palkovic et al., 2020). Tidal volume depends on direct projections from the retrotrapezoid nucleus to the preBötzinger Complex neurons. Respiratory chemodrive results from the activation of chemoreceptors in the brain stem and the carotid body by elevated PCO₂ and hypoxia. Hypoxia and hypercapnia cause significant increases in minute ventilation via increased activity in the carotid and the nucleus of the solitary tract. A significant component of respiratory chemodrive originates in the retrotrapezoid nucleus, which contains chemosensitive neurons, and integrates the peripheral chemoreceptive inputs from the carotid body (Palkovic et al., 2020).

Opioids reduce the respiratory rate from direct effects on the preBötzinger Complex and depression of the Parabrachial/Köllicker-Fuse Complex, which provides the excitatory drive to preBötzinger Complex neurons mediating the respiratory phase-switch. Opioids also depress the "awake drive" and chemodrive. Opioids also dose-dependently cause sedation, and this effect reduces or eliminates excitatory inputs to the brain stem (Palkovic et al., 2020).

Opioid-induced respiratory depression is dose-dependent, and the magnitude of depression correlates with the level of sedation (Palkovic et al., 2020). Opioids can cause mild sedation and hypoventilation with a PCO₂ above 50 Torr (mm Hg) at standard analgesic doses.
(Palkovic et al., 2020). However, at this level, patients can be prompted to breathe by voice or touch. With more profound sedation, painful stimuli still elicit respiration in patients. However, at very high opioid doses, $\text{PCO}_2$ exceeds 60 Torr, whereby severe hypoxia and hypercapnia, nor pain will be able to elicit respiratory efforts by the patient (Palkovic et al., 2020). Respiration is an automatic process that ensures oxygen uptake and carbon dioxide removal from the body. The primary drive to breathe derives from central chemoreceptors in the brain (Palkovic et al., 2020). In the awake state, the cortico-limbic system of the forebrain influences respiration and respiratory activity, which changes with the level of physical activity, emotions, and arousal. When the "awake drive" is lost during sleep, there is a decrease in respiratory minute ventilation and a reduced hypoxic ventilatory response (Palkovic et al., 2020).

**PONV**

Post-operative nausea and vomiting is a complication of general anesthesia. Contributing factors to PONV involve patient-specific factors such as being female, less than 50 years of age, non-smoking status, having a history of motion sickness, and having a history of PONV with past surgeries. Additionally, anesthesia-related factors such as volatile agents and opioid analgesics administered intra-operatively and post-operatively are associated with PONV. Volatile anesthetics and opioids set off the complex cascade that induces PONV, affecting the chemoreceptor trigger zone (CTZ) and subsequently causing PONV. Surgical-related factors also play a crucial role, such as the length and type of surgery, with each prolongment of 30 minutes increasing the risk of PONV by 60%. This prolonged time under general anesthesia combined with opioid use during this timeframe would contribute to post-operative nausea and vomiting (Elvir-Lazo et al., 2020).

**Gastrointestinal Tract**
Opioids decrease peristalsis by inhibiting the central and peripheral nervous systems. Most opioids decrease gastric motility by stimulating \( \mu \) receptors in the gut that cause increased contractions of muscles in the antrum and the upper duodenum. Opioids also act on the spinal cord and brain to suppress intestinal motility. Additionally, opioids block the intestines' peristaltic reflex by stimulating receptors in the enteric nervous system (ENS) and inhibiting nicotinic post-synaptic receptors. The ENS is a division of the peripheral nervous system that controls gastrointestinal behavior independently of the central nervous system. Decreasing peristalsis in patients may lead to aspiration risk and increased length of postoperative care (Khansari et al., 2013).

Opioids suppress antibody and cellular immune responses in the CNS and PNS, where the hypothalamic-pituitary-adrenal axis and autonomic nervous system are involved. For example, stimulation of \( \mu \) receptors decreases NK cell activity, macrophages, and T-cell proliferation release, all immunological components needed to resist bacterial infections. Decreasing this resistance may make patients prone to bacterial infections and increase their length of stay in the hospital (Khansari et al., 2013).

**Non-Opioids**

To combat opioid side effects, clinicians have tried proactively managing pain while limiting opioid consumption during the perioperative period through various multimodal plans. Multimodal analgesics can provide an alternative to offset the increase in opioid use. Many combinations are used to achieve this goal, and only a few are outlined below (Giovannitti et al., 2015).

*Alpha-2 Adrenergic Agonists*
In recent years, alpha-2 agonists have been a focal point of multimodal plans (Giovannitti et al., 2015). Alpha 2 adrenergic receptors play a crucial role in centrally inducing sedation via the locus coeruleus in the brain and mediating pain modification via the dorsal horn in the spinal cord when activated (Naja et al., 2014). Alpha-2 agonists also inhibit norepinephrine release from the presynaptic sympathetic neuron, which may reduce systemic vascular resistance and heart rate. Alpha 2 agonists are particularly useful in reducing the stress response and controlling cardiovascular parameter fluctuations intraoperatively for patients with a risk of cardiac morbidities (Giovannitti et al., 2015).

Dexmedetomidine, an opioid-sparing analgesia, is a highly selective alpha-2 agonist that has shown promising results in lowering pain perioperatively, reducing delirium, and preventing respiratory depression (Giovannitti et al., 2015). As with other alpha-2 agonists, it stimulates alpha-2 receptors in the dorsal horn of the spinal cord, inhibiting nociceptive neuron firing, which reduces the release of substance P. Initially, dexmedetomidine acts on the alpha-2 receptors of vascular smooth muscle, causing vasoconstriction and reflex bradycardia with rapid administration of large doses. However, after the initial effect, a more gradual central effect results in decreased sympathetic outflow and circulating catecholamine levels, causing decreased heart rate and blood pressure, which can aid in the sympatholytic effects of surgery intraoperatively and during emergence. Dexmedetomidine has a rapid distribution half-life of 6 mins and a terminal half-life of 2 hours, and it is highly lipophilic. It will likely be taken up by the fatty tissue in the morbidly obese population, thus prolonging postoperative analgesia and less opioid consumption and PONV in the PACU from opioid use. Though dexmedetomidine does carry similar sedation effects to opioids, it preserves the respiratory drive, giving more of a
benefit of use to a patient population pre-conditioned for respiratory depression (Giovannitti et al., 2015).

**Acetaminophen**

Acetaminophen or paracetamol is a commonly used analgesic drug in a multimodal approach to reduce opioid consumption postoperatively due to its similar central effects to opioids. Acetaminophen's exact mechanism of action remains unclear, and it has been categorized with NSAIDs because it inhibits the cyclooxygenase (COX) pathways. Acetaminophen inhibits the COX pathway in the central nervous system but not the peripheral tissues. Reduction in the COX pathway activity inhibits the synthesis of prostaglandins in the central nervous system, leading to analgesic effects. Thus, acetaminophen should be given preemptively to block the synthesis of prostaglandins before they are created through painful stimuli. The appropriate dose for preemptive analgesia is 1000 mg IV for approximately 20 minutes. The analgesic effect begins in 5 mins and peaks in 1 hour with a duration effect of 4-6 hours (Bohringer et al., 2019).

**Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)**

In contrast to acetaminophen, true NSAIDs inhibit the sensitization of pain receptors by blocking the inflammatory cascade both centrally and peripherally during painful stimuli such as surgery. Ibuprofen is a propionic acid derivative with anti-inflammatory, analgesic, and antipyretic properties similar to other nonspecific COX enzyme inhibitors. The compounded effect of blocking anti-inflammatory markers peripherally and centrally may yield less opioid consumption intraoperatively (Bohringer et al., 2019).

Ketorolac is another commonly used NSAID given intraoperatively due to its desirable characteristics in managing post-operative pain. It is important to note that ketorolac is avoided
in RYGB surgeries because of the increased risk of peptic ulcers. However, Skoger & Sundbom (2021) concluded in their retrospective study of 41,380 patients undergoing laparoscopic bariatric surgeries (37,913 RYGB, 3,467 SG) between 2010-2015 that temporary NSAID use (<30 days) did not increase the risk for peptic ulcers. The results supported that continuous NSAID administration (greater than 30 days) was a strong risk factor for developing peptic ulcers (Skogar, M. L., & Sundbom, M. 2022).

**Ketamine**

Ketamine is another analgesic drug that has proven beneficial in this patient population. Ketamine is an N-methyl-D-aspartate (NMDA) receptor antagonist with a half-life (2-3 hours), so it is reasonable to administer it via IV bolus rather than continuing infusion (Bohringer et al., 2019). Glutamate release from noxious stimuli activates NMDA receptors in the brain and spinal cord, signaling pain. Blocking these receptors prevents glutamate release and blocks the body's ability to recognize pain. Ketamine also presents other advantages in obese patients as it causes minor respiratory depression and elevates blood pressure and heart rate, contributing to improved minute ventilation and cardiac output. Given the predisposed decrease in functional residual capacity and increased need for cardiac output, ketamine may be an ideal drug for these patients. However, bolus doses should be limited to 0.25 mg/kg in patients with coronary artery disease to prevent tachycardia and hypertension. Some patients have incurred emergence delirium and hallucinations after ketamine administration, but this tends to incur when the dosing is greater than 0.5 mg/kg. In addition, the administration of midazolam 1 -2 mg given on induction prevents psychomimetic reactions and reduces the emergence delirium often associated with ketamine (Lam & Mui, 2016).

**Benzodiazepines**
Midazolam, a member of the Benzodiazepine class, provides anxiolytic and sedative properties for patients undergoing surgery and reduces the emergence delirium associated with ketamine. However, it should be used with caution in this patient population. The administration of benzodiazepine has been shown to depress the central respiratory drive and chemoreceptor responsiveness to hypercapnia (Giovannitti et al., 2015).

**Local Anesthetics**

Lidocaine infusions can be utilized in multimodal pain management. Lidocaine exerts its analgesic effects through several mechanisms. First, through the inhibition of sodium channels, lidocaine inhibits the nociceptive action potential propagation and neuronal excitability of peripheral impulses to the central nervous system. Lidocaine also works on N-methyl-D-aspartate receptors (NMDA) by inhibiting protein kinase C, causing a decrease in the post-synaptic depolarization of the NMDA receptors. The NMDA receptors are the primary channels responsible for excitatory neurotransmission and the afferent pain pathways to the brain.

Lidocaine also works on G-protein-coupled receptors. Specifically N-type voltage-gated calcium channels. The heterotrimeric G protein-coupled receptors (GPCRs) are widely distributed throughout the peripheral and central nervous system and are closely associated with the modulation of pain transmission. In neurons, calcium entry through calcium channels is essential for synaptic transmission. Voltage-gated calcium channels (VGCCs) are fundamental components of the presynaptic release through which neurotransmitter release can be modulated. Though there are five subtypes of VGCCs, N-type are found in the spinal cord, and blocking these channels produces profound analgesic effects (Yang et al., 2020).

Local anesthetics in the form of regional anesthesia may benefit the multimodal approach for bariatric procedures, specifically ultrasound-guided transversus abdominis plane (TAP).
block. A TAP block involves the injection of a local anesthetic solution into a plane between the internal oblique muscle and the transversus abdominis muscle. The thoracolumbar nerves originating from T6- L1 spinal roots are found in this plane and are responsible for the supply of sensory nerves of the anterolateral abdominal wall. Thus, local anesthetic spread through this plane blocks the neural afferents of this region, providing analgesia to the anterolateral abdominal wall. Providing analgesia to this region may reduce the number of opioids needed for pain control, thus, preventing post-operative complications such as respiratory depression and PONV (Tsai et al., 2017).

**Beta-Adrenergic Antagonists**

Beta-adrenergic antagonists, such as esmolol, have been used in some studies for analgesia. The mechanism of action concerning analgesic effects is not yet known. Several hypotheses have been brought forth, such as the inhibition of sodium channels and, thus, the facilitation of inhibitory neurotransmitter release. In contrast, others postulate that analgesic effects involve blocked tetrodotoxin-resistant sodium channel activity in the dorsal root ganglion neurons. Others point to facilitating inhibitory transmitter release through calcium entry but in a Beta1-adrenoceptor- independent manner as producing the antinociceptive effect (Giovannitti et al., 2015).

**Corticosteroids**

Dexamethasone is a corticosteroid typically given intraoperatively to reduce surgery-induced inflammation through its effects of inhibiting prostaglandin synthesis, which reduces postoperative nausea and vomiting. Additionally, dexamethasone possesses analgesic properties by inhibiting phospholipase, which is necessary for the inflammatory chain reactions that elicit
immune responses to pain in both the COX and lipoxygenase pathways (Skogar, M. L., & Sundbom, M. 2022).
Literature Review

Methodology

A literature review was performed utilizing the following databases: PubMed, Springer Link, and Google Scholar. Prospective, quantitative, randomized control trials (RCT), retrospective, and systemic reviews of studies published within the last five years, 2017-2022, were preferentially selected. Lower levels of evidence, such as observational case studies, literature reviews, and non-experimental studies, were utilized in the search to support the literature found. Initially, twenty articles were selected for review, and five were excluded due to duplicate studies. Initial search for keywords included "ERAS protocols, opioids, and bariatric surgery," which provided various articles regarding the use of opioids in bariatric surgeries and the complications associated with narcotics. Further search terms were more specific and related to "length of stay with opioids and bariatric surgery," "adjuncts for pain relief in post-operative bariatric surgery," and "complications of post-operative nausea and vomiting with opioids in bariatrics," which yielded more results related to the research question.

The literature review noted that antiemetics dose and timing are crucial in preventing PONV. Additionally, research has highlighted that certain pain adjuncts, along with opioids, are beneficial to promoting lower pain scores in patient satisfaction surveys, but may contribute to more sedation, thus increasing the length of stay in the PACU setting. Lastly, research has scrutinized the anesthetic plan used in bariatric patients (i.e., volatile anesthetics vs. total intravenous anesthesia (TIVA) as a contributory factor to PONV, pain scores, and opioid consumption in the post-operative period.
PONV

Recognizing the PONV risk factors, Naeem et al. (2020) completed a systematic review of studies starting in 2010. The authors narrowed their search to 12 randomized control trials (RCT) and 9 observational studies, 15 of which involved laparoscopic gastric procedures and 12 of which involved the use of opioids perioperatively. The systematic review concluded that a multi-agent approach with dexamethasone combined with one or more antiemetic agents from a different class provided better results than one alone. Two studies specifically highlighted that the use of dexamethasone 8 mg, haloperidol 2 mg, and ondansetron 8 mg yielded less nausea ($p < .015$) and vomiting ($p < 0.1$) during the first 36 hours post-operatively compared with ondansetron alone. Additionally, administering aprepitant 80 mg, a neurokinin-1 antagonist, given orally one hour before surgery, and ondansetron 4 mg intravenously prior to surgery resulted in lower incidences of vomiting 72 hours post-operatively when compared to ondansetron 4 mg given alone (Naeem et al., 2020).

Ashoor et al. (2022) performed a randomized, double-blind study including 90 patients undergoing laparoscopic sleeve gastrectomy. Participants had a BMI $> 35 \text{ kg/cm}^2$, were between the ages of 25-55, and had well-controlled hypertension or diabetes. The patients split into three groups: the A/D group received 80 mg aprepitant and 8 mg dexamethasone, the M/D group received 30 mg mirtazapine (an anti-depressant) and 8 mg dexamethasone, and the D group only received 8 mg dexamethasone. During the early post-operative period (0 - 24 hrs), there was a significantly lower number of vomiting incidences and rescue antiemetics use in the A/D and M/D groups compared to the D group alone. Only 10.3% of the A/D group and 10.7% of the M/D group used rescue antiemetics compared to 30% of the D group, and only 10.7% of the M/D group had an occurrence of vomiting compared to 20.7% of the D group with no
occurrences in the A/D group. Another finding in the study pointed to the analgesic effects of aprepitant and mirtazapine, with differences in pain scores found among the groups. At 2-24 hours (hrs), the pain scores were 2.3 (±0.5) in the A/D group, 3.8 (±0.4) in the M/D group, and 4.3 (±1.1) in the D group ($p < .0001$). Another variable showed that the patient sedation scores were much higher in the M/D group than in the other two groups. Mirtazapine is well known to alleviate preoperative anxiety but can cause a higher incidence of post-operative sedation in patients as well, and those results coincided with this study (Ashoor et al., 2022).

Similar to Ashoor et al. (2022), Therneau et al. (2017) reviewed the medical records of 338 female patients undergoing laparoscopic bariatric surgery between 2014-2016 to determine the significance of administering multiple antiemetics to reduce PONV associated with intraoperative fentanyl and hydromorphone. Therneau et al. (2017) compared using 40 mg of aprepitant as a multimodal adjunct to triple antiemetic prophylaxis (dexamethasone, droperidol, and ondansetron). Of the 338 patients, 172 (51%) received the aprepitant with the triple antiemetic prophylaxis, while 166 (49%) only received the triple antiemetic prophylaxis. The PONV rates were 11% and 17% among the aprepitant and no-aprepirtant groups, respectively. Within one hour after PACU discharge, the aprepitant group reported 19% PONV versus the no-aprepirtant group at 31%. However, within 48 hrs of PACU discharge, the percentages of PONV were similar between both groups within the 60% range. The episode of vomiting within that time was substantially less in the aprepitant group at 6% vs. the no-aprepirtant group at 13% (Ashoor et al., 2022).

Bamgbade et al. (2017) highlighted a similar significance of increasing the number of intraoperative antiemetics to reduce PONV with their observational clinical study of the perioperative data of 400 consecutive laparoscopic bariatric surgery patients over six years. The
mean age was 42 (±8) years, the gender ratio favored women to men (4:1 ratio), and the BMI range was 39-80 kg/m² with a mean of 49 (±7). The authors reviewed the use of prochlorperazine, a dopamine receptor antagonist, and cyclizine, a histamine receptor antagonist, in conjunction with ondansetron and dexamethasone to observe the patient outcomes in terms of PACU duration, PONV, and analgesia within the first 24 hours. Various combinations were used, with one group only receiving ondansetron solely. In contrast, the other groups received a combination of either dexamethasone with cyclizine and ondansetron, dexamethasone and ondansetron, or dexamethasone with cyclizine and prochlorperazine. The prophylaxis combination of dexamethasone and cyclizine with prochlorperazine provided the best clinical outcomes, with 97.6% reporting shorter PACU durations, categorized as < 50 minutes, and 100% of patients reporting zero PONV (Bamgbade et al., 2017).

The study by Bamgbade et al. (2017) also highlighted that a multimodal intraoperative analgesia approach with a multimodal antiemetic limited the incidence of PONV within 24 hours instead of using morphine alone. Different combinations of morphine, acetaminophen, tramadol, parecoxib (COX-1 inhibitor), and diclofenac (COX-1 and COX-2 inhibitor) determined this result. Inhibition of cyclooxygenase 1 (COX-1) and cyclooxygenase 2 (COX-2) prevents the formation of prostaglandins, which are mediators of pain and inflammation, thus, reducing the amount of opioid consumption among patients. Compared to several multimodal analgesia modes, tramadol with acetaminophen and diclofenac provided the best outcome, with the least reported incidence of PONV ($p = 0.001$) (Bamgbade et al., 2017).

**Opioid Free Analgesia vs Opioid Use**

Multimodal analgesia utilizes opioids with other analgesics. To determine if opioid-free anesthesia (OFA) was better than multimodal analgesia (MMA) for patients undergoing a
laparoscopic gastric sleeve, Ibrahim et al. (2022) undertook a single-blinded randomized control test of 103 participants at one institution. All the patients received induction with IV propofol (2 mg/kg), muscle relaxation with cisatracurium (0.15 mg/kg), and sevoflurane for anesthesia in addition to an ultrasound-guided bilateral oblique subcostal transverse abdominis plane (TAP) block. The patients in the OFA group received the following doses of non-opioids: IV dexmedetomidine infusion at 0.5 mcg/kg/hr, IV ketamine infusion at 0.5mg/kg/hr, and IV lidocaine infusion at 1mg/kg/hr in addition to a TAP block, while the MMA group only received a fentanyl dose of 1mcg/kg at an induction in addition to a TAP block. The study's primary outcome centered around the patients' quality of recovery at the sixth and 24th hours post-operatively.

The Quality of Recovery 40 (QoR-40) questionnaire assessed the quality of recovery by scoring the patients' post-operative emotion, physical independence, psychological support, and verbalized pain rating. The patients carried out the predetermined questionnaire verbally, signaling that the higher the score, the more favorable the recovery. The secondary outcomes focused on post-operative opioid consumption, time to ambulation, and discharge readiness from the PACU. The study concluded that at the sixth-hour mark, the QoR-40 survey was higher in the OFA group than the MMA group ($p <.0001$) with no difference noted at the 24th hour (Ibrahim et al., 2022).

Regarding the secondary outcomes, pain levels, and morphine consumption were significantly higher in the MMA group vs. the OFA group (20 mg vs. 10 mg; $p = 0.0005$), and readiness for discharge times (505 vs. 444 mins) and difference in time to ambulation between the two groups had little difference. The study highlighted a reduction in readiness to discharge
by 21% and improved recovery satisfaction scores with the opioid-free anesthesia vs. the multimodal analgesia plan (Ibrahim et al., 2022).

Judith et al. (2021) conducted a retrospective study to evaluate the analgesic effects of OFA vs. opioid base anesthesia (OBA) in patient recovery for patients undergoing laparoscopic gastric sleeve gastrectomy surgery between June 2018 and September 2019. Of the participants, 81% were female, and the median age and BMI were 41 and 42.85, respectively. The anesthetic maintenance in the OFA group was a propofol infusion of 90-200 mcg/kg/min with one or more of the following IV infusions: dexmedetomidine (0.2-0.6 mcg/kg/hr), lidocaine (0.5-2 mg/kg/hr), or ketamine (0.5 mg/kg) IV bolus as an adjunct to the infusions. The OBA group received sevoflurane or propofol infusion set at (90-200 mcg/kg/min) with intermittent fentanyl boluses or a continuous remifentanil infusion set at 0.05-0.3 mcg/kg/min. The results were similar in pain scores and PONV incidences in the 6-24 hours post-operatively. Furthermore, opioid consumption was similar in both groups in the first 6 hours post-operatively, with median scores showcasing 11.25 in the OFA group versus 10.0 in the OBA group ($p = 0.82$). Likewise, following the 6 to the 24-hour mark, there was no reporting of opioid consumption ($p = 0.79$). Lastly, no difference was observed concerning overall hospital length of stay; only the readiness to discharge from PACU was quicker in the OFA group (Judith et al., 2021).

**Reducing Pain Severity and Opioid Consumption**

Chaouch et al. (2022) conducted a systematic review and meta-analysis to compare the efficacy of ketamine for pain management following bariatric surgery with a placebo. The review retained seven randomized control trials published between 2009 and 2021. Three RCTs used only one bolus of ketamine, three used a ketamine bolus and infusion, and only one used a ketamine infusion without a bolus. The bolus doses were all under 0.5 mg/kg, and the infusion
rates were 1 mcg/kg/min. The review included 412 patients (202 patients in the ketamine group and 210 patients in the control group) between the ages of 28-45.5 years old with a mean BMI between 41-53.5 kg/m². The review's primary outcome was total opioid consumption in IV morphine equivalents during the first 24 hours after surgery. Chaouch et al., 2022, observed a significant reduction in total opioid consumption in the ketamine group ($p = 0.01$). It is also important to note that there was no difference in the findings between the groups that received infusions or just a bolus (Chaouch et al., 2022).

Okut et al. (2022) conducted a prospective, randomized, double-blind control trial on patients with morbid obesity who underwent laparoscopic SG between April 2019-October 2020. Ninety-two patients with a mean age of 34.7 years and a mean BMI of 42.5 kg/m² were included in this trial. The participants split into two groups: group I had an ultrasound-guided TAP block with 30 mL 0.5% bupivacaine upon completion of surgery before recovery from general anesthesia, and group II did not receive a TAP block. Post-operative pain was treated with a patient-controlled analgesia (PCA) device set to infuse 25 mg of tramadol as a bolus with a lockout time of 20 minutes. Visual Analog Scores and PCA requirements recorded pain over 24 hours post-operatively. The pain scores were significantly lower in group I within the first 6 hours, 12 hours, and 24 hours post-operatively. Additionally, PONV scores after 24 hours were significantly lower in group I. However, both groups had similar hospital stays (Okut et al., 2022).

Sun et al. (2022) conducted a single-blind, prospective, randomized controlled trial to investigate the analgesic effect of a lidocaine infusion compared with TAP blocks. Patients between the ages of 18-65 years with a BMI ≥35 kg/m² undergoing laparoscopic bariatric surgery were included. Ninety-nine patients were randomized into 3 separate groups: a lidocaine
group, a TAP block group, or a control group that received neither intervention. The lidocaine group was given a loading dose of 1.5 mg/kg on induction, followed by 2 mg/kg/hr maintenance infusion until the end of surgery. The TAP block group was administered a bilateral dose of 20 mL 0.25% ropivacaine after induction of general anesthesia. The control group received general anesthesia only. During the procedures, propofol and remifentanil were infused with sevoflurane as the anesthetic. Intraoperatively, less remifentanil and propofol were used in the lidocaine and TAP block groups than in the control group \( p < 0.010, p = 0.002, \) respectively. The primary outcomes were pain levels and opioid consumption post-operatively. Compared with the control group, there was significantly less pain reported among the lidocaine and TAP block groups \( p = 0.002 \) and \( p = 0.003 \), respectively), with no difference reported between the lidocaine and TAP block group in the first 12 hours post-operatively. However, significantly less pain was reported among the lidocaine group than the TAP block group between 12-24 hours post-operatively \( p < 0.0166; \) Sun et al., 2022

De Morais et al. (2020) conducted a randomized, double-blind, placebo-controlled study on patients undergoing RYGB to determine if esmolol infusions intraoperatively would reduce opioid consumption. The participants included 40 patients between 18- 50 years old with a BMI > 40kg/m². Group 1 received a 0.5 mg/kg bolus of esmolol in 30 mL of saline before induction of anesthesia, followed by an infusion at 15 mcg/kg/min until the end of surgery. Group 2 patients received only 30 mL of saline as a bolus, followed by an infusion of saline. Other anesthetic medication for these surgeries included fentanyl (3 mcg/kg), propofol (2-4 mg/kg), rocuronium (0.6mg/kg), and sevoflurane at 2% with remifentanil infusions if the heart rate was 15% higher or the systolic blood pressure was 20% higher than baseline. The primary objective was to evaluate pain intensity over 24 hours, remifentanil consumption during surgery, and
morphine consumption post-operatively. Remifentanil supplementation was drastically reduced intraoperatively, with only 3 patients requiring supplementation in the esmolol group compared to 17 in the control group ($p=0.0001$). Additionally, pain intensity was lower in the esmolol group up to 24 hours post-operatively (De Morais et al., 2020).

Lee et al. (2019) performed a meta-analysis of double-blinded, randomized control trials to assess the effect of IV acetaminophen compared to a placebo for pain management in bariatric surgery. Four RCTs including 349 patients with a BMI > 40 kg/m$^2$ or > 35 kg/m$^2$ with obesity-related comorbidities were chosen. 175 patients were provided IV acetaminophen, and 174 were provided a placebo. All trials used 1000 mg of IV acetaminophen every 6 hours for 1 day as an intervention and IV saline placebo every 6 hours for 1-day control. The primary outcomes measured VAS scores 24 hours after surgery and post-operative opioid consumption in morphine-equivalent doses. Due to the heterogeneity of different types of opioids administered (ex. hydromorphone, morphine, oxycodone, and fentanyl), opioids other than morphine were converted to morphine equivalent dose (MED) using a standard conversion factor. Compared to the placebo group, the IV acetaminophen group had a significantly lower post-operative pain score by 0.66 points, $p<0.001$ 24 hours after surgery. The IV acetaminophen group had significantly lower post-operative opioid use than the placebo group by 6.44 mg MED (Lee et al., 2019).

**Discussion**

**PONV Reduction**

Naeem et al.’s (2020) systematic review regarding using more antiemetics showcased the benefits of preventing PONV by utilizing more than one agent. However, the authors admit that the study presented several limitations. First, the sample size was small, with only 21 studies;
approximately 40% of these studies were observational and held within one institution. Given these limitations, it took much work for the authors to overcome the heterogeneity in outcome reporting (Naeem et al., 2020).

Similarly, the randomized, double-blinded test performed by Ashoor et al. (2022) involved a small sample size at only one institution, so the possibility of bias could not be ruled out. Secondly, the baseline risk of PONV was not evaluated due to the use of dexamethasone, a baseline antiemetic. Finally, the groups were not matched for comorbidities (Ashoor et al., 2022). Therneau et al. (2017) also pointed out the limitations of bias in their study. The authors noted that the determinant of PONV was reliant on the patients self-reporting. The authors believed that patients may have overestimated in anticipation of nausea before an actual onset, and others may have underestimated nausea and thereby withheld treatment (Therneau et al., 2017).

Bamgade et al. (2017) is an observational study considered inferior to an experimental study. The targeted population regarding patient factors such as age, gender, and BMI are desirable with valid results. However, the surgical-related factors, such as what type of laparoscopic bariatric surgery and locational setting, were distinguished within the results, and the population size was only 400. The authors agreed that the study highlighted multimodal antiemetics, but more extensive randomized control studies would produce more significant results (Bamgbade et al., 2017).

**OFA vs Opioid Use**

Ibrahim et al. (2022) involved a lower level of evidence since the RCT involved a small sample size of 103 participants at one specific institution. The results could be biased to surgeons operating, and facility standards may differ at other institutions. As a result, there were some
other inherent limitations to the study, such as the actual survey questions that needed to be discovered, so unable to gauge the questions posed that would merit proper metrics of quantifiable pain by the patients. Finally, the use of regional anesthesia may have altered the results. Avoiding a TAP block may have contributed to higher pain scores reported among the participants (Ibrahim et al., 2022).

Judith et al. (2021) retrospective study was met with limitations. First, the study only reviewed two surgeons at one specific institution. Second, the nonrandom assignment of patients to the groups may have introduced selection bias among anesthesiology providers. Finally, as a retrospective study, knowledge regarding patients’ charts was limited, so the authors could not discern previous opioid use and baseline pain scores among the participants (Judith et al., 2021).

**Reducing Pain Severity and Opioid Consumption**

Chaouch et al.’s (2022) systematic review with meta-analysis of RCTs comparing ketamine infusion or bolus with placebo for pain management following bariatric surgery demonstrated that the administration of ketamine lowered opioid consumption during the first 24 hours postoperatively. However, the heterogeneity of opioids used as supplemental analgesia may have altered the data. Some RCTs used acetaminophen with opioids which may have reduced opioid consumption. Additionally, only acute management was assessed, so further trials studying the impact of ketamine on chronic pain are needed (Chaouch et al., 2022).

Okut et al.’s (2022) prospective randomized clinical trial showed that TAP blocks with bupivacaine reduce postoperative analgesia in morbidly obese patients. However, there were some limitations. First, the sample size was minimal, with only 60 patients included. Second, the TAP block effectiveness depends on the provider’s skill level. Needle placement sites are empirical regarding dermatomes and may lead to different results.
Sun et al.’s (2022) single-blind, prospective, randomized control trial found that IV infusions of lidocaine or ultrasound-guided TAP block improved postoperative pain scores vs. the control group receiving only general anesthesia. The study also observed a lower prevalence of PONV in the lidocaine and TAP block groups, which could have resulted from the lower opioid consumption perioperatively. The results could have signified the limits in the duration of action of the TAP block regarding the ropivacaine administered. The authors highlighted that the dose of ropivacaine was effective for immediate postoperative pain. However, the most effective amount of local anesthesia needed for postoperative pain remains controversial and thus has not been determined yet (Sun et al., 2022).

De Morais et al.’s (2020) randomized, double-blind, placebo-controlled study showed that intraoperative esmolol reduces pain intensity and remifentanil consumption during RYGB. However, the study may have altered pain intensity scores postoperatively. The reduction in intraoperatively remifentanil consumption may have led to lower pain scores postoperatively because remifentanil is known to cause hyperalgesia after discontinuation.

Lee et al.’s (2019) meta-analysis concluded that IV acetaminophen after bariatric surgery effectively reduces postoperative pain scores and opioid doses in obese patients. The study was met with some limitations. First, the sample size was small, with only 349 patients. Second, IV acetaminophen was only compared to a placebo, so it also lacked comparisons to ibuprofen or other analgesics. Finally, the opioid regimens postoperatively varied greatly between trials. They included morphine, hydromorphone, fentanyl, and oxycodone. While the regimens were converted to morphine-equivalent doses, this conversion may not have represented the duration of action of each opioid used (Lee et al., 2019).
Conclusion

Recommendations

The research needs to be more inclusive, with larger sample sizes from various hospitals, with specific opioids used to gauge the appropriate multimodal approach. For example, Judith et al.’s (2021) retrospective study concluded no difference in reducing pain scores when opioids were used instead of an opioid-free anesthesia model. This conclusion could have primarily resulted from nonrandom assignments that allowed selective bias from anesthesiologists at one institution to affect the result (Judith et al., 2021). In addition, Lee et al.’s (2019) meta-analysis only compared IV acetaminophen to an opioid regimen that they converted to a morphine scale; thus, this may not have been accurate since the various opioids used in the study have different durations of action, and may not have offered an accurate comparison to acetaminophen and opioids (Lee et al., 2019).

Importance to Anesthesia Practice

Bariatric surgeries are performed in many settings around the world daily. With obesity on the rise, many anesthetists will confront these surgeries (or other surgeries not centered around weight reduction), dealing with this population frequently. Given the surgical risks around bariatric surgeries, clinicians must utilize the best possible techniques and reduce the amount of opioid use in this population to reduce hospital costs and adverse outcomes (Kassir et al., 2016).

In 2011, The National Academy of Medicine reported that pain costs the nation $635 billion annually in medical treatment and lost productivity. Patients undergoing surgery have an increased risk of chronic opioid use during the first year of surgery compared to the nonsurgical population because providers are incentivized to overestimate posthospital opioid needs to
reduce the length of hospital stay (Stone et al., 2017). The lack of treating pain effectively has led to the unintended consequences of more opioid utilization among this population. Increased opioid use increases the potential for adverse effects such as respiratory depression, suppressed gastric motility, delayed wound healing, and increased PONV. These adverse effects increase the length of stay in hospitals and could harm patients (Khansari et al., 2013).

Opioids may have their place in anesthesia and sometimes may be utilized effectively. However, the problem occurs when anesthesia relies more on narcotics than an MMA approach. Reliance on narcotics can increase hospital costs and patients' pain scores, thereby increasing the length of stay and possibly contributing to adverse outcomes intraoperatively and post-operatively. Alternatives to opioids have dramatically lowered the patient length of stay by promoting early ambulation, lowering PONV, and decreasing reliance on opioid use following surgery in the PACU, which has provided lower costs to the hospital facilities and resulted in favorable patient satisfaction scores (Stone et al., 2017). Additionally, clinicians have provided a safer environment for patients while reducing risks intraoperatively and emergently by reducing risks associated with opioids, such as respiratory depression. Though many facilities have adopted a drastic reduction in opioids through established ERAS protocols, more needs to be done in this field. With more research on pain alternatives, clinicians will better understand how to use the currently available anesthesia tools and look to the forefront of new alternatives introduced to reduce opioids (Stone et al., 2017).

There is a rise in the morbidly obese population, and the social and behavioral trends continue to perpetuate higher numbers. Bariatric surgery is justified as it improves weight loss, increases life expectancy, and reduces comorbidities associated with obesity (Lee et al., 2016). Morbid obesity brings a host of inherent surgical risks that increase the incidence of
complications and, in some cases, mortality (Lee et al., 2016). Opioid anesthesia, as this population's sole analgesia provider, only exacerbates surgical complications and delays recovery times, providing an ever-concerning safety risk to the patients and a burgeoning financial burden to hospitals (Stone et al., 2017). Clinicians recognize the need for alternatives and have looked to utilize a multimodal approach to combat the problem (Stone et al., 2017). Adjunct medications such as those referenced above provide a synergistic approach to treating pain while reducing opioid consumption, thus, reducing patient length of stay from oversedation and cardiorespiratory depressants. Local anesthetics, specifically regional anesthesia, have also contributed to opioid reduction while providing improved recovery times and higher patient satisfaction scores when used with opioids or as a standalone treatment for pain during surgery (Tsai et al., 2017). Though more new multimodal approaches are coming to the forefront, the one constant remains: a decline in opioid use is strongly encouraged to reduce their adverse effects in this patient population.
References


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