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Abstract

Background: Postoperative pain and opioid use are central concerns following modified radical mastectomy (MRM), a procedure commonly performed for breast cancer treatment. Effective pain management is crucial for enhancing recovery, reducing hospital stays, and minimizing the transition to chronic pain states. Traditionally, general anesthesia (GA) has been the standard technique for MRM. However, regional anesthesia approaches, especially thoracic spinal anesthesia (TSA), have gained traction due to their potential to reduce acute postoperative pain, decrease opioid consumption, and limit associated adverse effects. This review explores the comparative effects of general anesthesia and thoracic spinal anesthesia on postoperative analgesia and opioid requirements following MRM. We begin by examining the epidemiology, causes, and pathophysiology of post-mastectomy pain, including the transition from acute to chronic pain and associated risk factors. Advances in anesthetic strategies are then discussed, including a detailed review of general and regional techniques such as thoracic paravertebral block, thoracic epidural, pectoral nerve blocks, serratus anterior plane block, and transversus thoracic plane block. Thoracic segmental spinal anesthesia is highlighted for its anatomical and physiological basis, indications, contraindications, complications, and clinical significance. Pharmacological agents commonly used in these techniques—including propofol, fentanyl, atracurium, bupivacaine, dexmedetomidine, and dexamethasone—are reviewed in detail, with attention to their mechanisms, clinical uses, adverse effects, and monitoring requirements. Clinical evidence comparing pain outcomes and opioid consumption between GA and TSA is synthesized, including secondary outcomes such as complications, recovery profiles, and patient satisfaction. Limitations of existing literature are acknowledged, and practical recommendations for anesthetic selection in MRM are provided. Finally, the review identifies key research gaps and suggests future directions to optimize perioperative analgesia and minimize opioid use. Conclusion: In summary, while both GA and TSA can provide effective anesthesia for MRM, emerging evidence favors thoracic spinal and other regional techniques for superior pain control and reduced opioid need. The choice of anesthetic should be individualized, balancing patient comorbidities, surgical factors, and institutional expertise, to maximize postoperative outcomes and long-term quality of life.

Keywords: Postoperative Analgesia, Opioid Use, Modified Radical Mastectomy

Mohammed Ashraf Saed et al.



Introduction

Modified radical mastectomy (MRM) remains a cornerstone in the surgical management of breast cancer, offering effective local disease control and improved survival. Despite its oncologic benefits, MRM is associated with substantial postoperative pain, which can adversely impact recovery, prolong hospitalization, and predispose to chronic pain syndromes. Traditional reliance on general anesthesia for breast surgery, though effective, often necessitates the use of systemic opioids, which carry risks of nausea, vomiting, sedation, respiratory depression, and potential for dependence. In recent years, there has been a paradigm shift toward regional anesthesia techniques, notably thoracic spinal anesthesia, driven by their potential to enhance postoperative analgesia, reduce opioid requirements, and mitigate perioperative complications. [1,2].

The aim of this review is to critically evaluate the comparative effects of general anesthesia and thoracic spinal anesthesia on postoperative pain and opioid consumption in patients undergoing MRM. While a growing body of evidence supports regional techniques, the optimal anesthetic approach remains debated, and research gaps persist regarding their long-term benefits, safety, and patient-centered outcomes. Addressing these questions is essential for refining perioperative care pathways, improving recovery trajectories, and minimizing the burden of opioid-related adverse effects in breast cancer surgery patients. This article synthesizes current evidence and provides practical insights for clinicians involved in the anesthetic management of MRM.

Post-Mastectomy Pain

Post-mastectomy pain is recognized as a complex, multidimensional phenomenon that can significantly affect physical function, emotional well-being, and overall quality of life in breast cancer survivors. The prevalence of moderate to severe pain within the first week after modified radical mastectomy (MRM) is reported to range from 40% to 60%, with a substantial proportion of patients experiencing persistent pain months or even years after surgery [1]. While acute pain is expected due to surgical trauma, the transition to chronic pain is a major concern that can impair daily activities, limit shoulder mobility, and contribute to psychological distress such as anxiety, depression, and insomnia [2].

The pain experienced after mastectomy often includes both nociceptive and neuropathic components. Nociceptive pain arises from tissue injury, inflammation, and muscle damage, while neuropathic pain results from direct nerve injury, particularly to the intercostobrachial nerve or other peripheral nerves during axillary dissection. Neuropathic features may include burning, tingling, shooting, or electric-like sensations, which are particularly distressing and challenging to manage with standard analgesics [3]. This dual nature of pain underscores the need for multimodal strategies that address both components for optimal recovery.

Persistent post-mastectomy pain can have far-reaching consequences beyond the immediate postoperative period. Chronic pain is associated with functional limitations, impaired sleep, reduced work capacity, and a heightened risk of opioid dependence. In addition, unresolved pain may interfere with adjuvant cancer therapies such as chemotherapy and radiotherapy, potentially impacting long-term oncological outcomes [4]. The burden of post-mastectomy pain thus extends beyond symptom control, representing a major target for improving survivorship care.

Despite advances in surgical technique and pain management, the incidence of postmastectomy pain remains unacceptably high, indicating that current approaches are insufficient for many patients. This ongoing challenge has fueled research into better perioperative analgesic strategies, including novel regional anesthesia techniques and

Mohammed Ashraf Saed et al.



individualized pain management protocols [5]. Understanding the clinical features and burden of post-mastectomy pain is the first step in developing effective prevention and treatment strategies.

Social, cultural, and psychological factors can also modulate the experience and reporting of post-mastectomy pain. Patients with higher levels of social support and effective coping strategies may experience less severe or less disabling pain. Conversely, those with a history of chronic pain, anxiety, depression, or catastrophizing are at increased risk of both acute and chronic pain syndromes after breast surgery [6]. These considerations highlight the need for comprehensive, multidisciplinary perioperative care that addresses both the physical and psychological dimensions of post-mastectomy pain.

Causes of Acute and Chronic Post-Mastectomy Pain

The causes of acute post-mastectomy pain are primarily related to the direct tissue trauma and inflammation resulting from surgical incision, tissue retraction, and dissection. During MRM, manipulation and removal of breast tissue, axillary lymph node dissection, and division of pectoral muscles all contribute to local nociceptor activation and acute inflammatory responses. Edema, hematoma formation, and seroma can exacerbate tissue distension and pain in the immediate postoperative period [7]. Acute pain typically peaks within the first 48 hours postoperatively, requiring effective management to prevent excessive sympathetic activation and delayed recovery.

Nerve injury is a critical factor linking acute surgical pain to the development of chronic pain syndromes. The intercostobrachial nerve, which provides sensory innervation to the upper medial arm and axilla, is particularly vulnerable during axillary clearance. Transection or stretching of this nerve can result in persistent numbness, paresthesia, or neuropathic pain that persists long after wound healing. Other nerves at risk include the medial and lateral pectoral nerves, long thoracic nerve, and thoracodorsal nerve, depending on the extent of dissection [8].

Chronic post-mastectomy pain is defined as pain that persists beyond three months after surgery and is not attributable to other causes such as infection, recurrence, or lymphedema. Chronic pain often has a neuropathic character and is believed to arise from maladaptive changes in both the peripheral and central nervous systems following nerve injury. Inflammatory mediators, changes in ion channel expression, and altered neurotransmitter release contribute to the sensitization of pain pathways and persistence of symptoms [9]. Some patients may also develop phantom breast pain, characterized by pain perceived in the absent breast tissue.

Risk factors for chronic post-mastectomy pain include the severity of acute postoperative pain, extent of axillary surgery, adjuvant radiotherapy or chemotherapy, genetic susceptibility, and pre-existing pain or psychological comorbidity. Importantly, inadequate control of acute pain is a modifiable risk factor and has been shown to increase the likelihood of chronic pain development [10]. This highlights the importance of aggressive perioperative pain management not only for immediate comfort but also for long-term outcomes.

Finally, it is increasingly recognized that the interplay between surgical technique, nerve preservation, and anesthetic management significantly influences the risk of persistent pain. Surgeons and anesthesiologists must collaborate closely to minimize nerve injury, employ minimally invasive techniques when feasible, and tailor analgesic strategies to the individual risk profile of each patient [11].



Pathophysiology and Risk Factors

The pathophysiology of post-mastectomy pain involves complex interactions between inflammatory, neural, and psychological processes. Surgical injury triggers the release of inflammatory cytokines, prostaglandins, and chemokines, which sensitize nociceptors and facilitate pain transmission. Damage to sensory nerves, such as the intercostobrachial nerve, leads to abnormal nerve regeneration, neuroma formation, and spontaneous ectopic firing, which are key features of neuropathic pain [12]. Central sensitization—where spinal dorsal horn neurons become hyperresponsive—plays a crucial role in amplifying pain signals, promoting allodynia and hyperalgesia that persist even after tissue healing. Multiple patient and surgical factors influence susceptibility to acute and chronic pain after MRM. Younger patients are at higher risk, possibly due to greater nerve plasticity or differences in pain perception. Female gender, pre-existing chronic pain, high preoperative pain scores, and psychological factors such as anxiety, depression, and catastrophizing have been consistently linked to greater pain severity and chronicity [13]. Surgical factors—including the extent of lymph node dissection, duration of surgery, and use of adjuvant therapies—also contribute to risk.

Genetic polymorphisms affecting inflammatory mediators, opioid receptors, and pain modulation pathways may further predispose some individuals to persistent pain. Studies have identified variations in genes encoding catechol-O-methyltransferase (COMT) and voltage-gated sodium channels as potential contributors to chronic pain risk after breast surgery [14]. The emerging field of pharmacogenomics may ultimately enable more personalized approaches to pain prevention and management in the surgical oncology population.

Radiotherapy and chemotherapy are independent risk factors for post-mastectomy pain. Radiation-induced fibrosis and nerve injury can exacerbate both nociceptive and neuropathic pain, while certain chemotherapeutic agents, such as taxanes, are associated with peripheral neuropathy. These factors necessitate ongoing pain assessment and multidisciplinary management in the months following surgery [15].

Effective perioperative analgesia is paramount for reducing both the severity and duration of postoperative pain. Multimodal approaches—including regional anesthesia, non-opioid analgesics, and psychological support—have demonstrated efficacy in lowering pain scores, opioid consumption, and the incidence of chronic pain syndromes. Early identification and intervention for high-risk patients are essential strategies for optimizing long-term outcomes after MRM [16].

Anesthesia for Breast Surgery

Modern anesthesia for breast surgery has evolved far beyond simply ensuring unconsciousness during the operation. The focus now includes optimal perioperative analgesia, early functional recovery, minimizing opioid use, and reducing the risk of chronic pain. Breast surgery patients—many of whom are older adults or have significant comorbidities—require tailored approaches that maximize safety while improving postoperative quality of life. A wide variety of anesthetic techniques are available, with the selection driven by patient factors, surgical extent, institutional protocols, and clinician expertise. Increasingly, evidence supports a multimodal, individualized approach that integrates both general and regional anesthesia techniques [17].

Historically, general anesthesia has been the mainstay for modified radical mastectomy (MRM) due to its simplicity, reliability, and ability to provide amnesia and immobility for the duration of surgery. The method is familiar to all anesthesiologists and is applicable to nearly all patient populations. However, the limitations of general anesthesia in terms of

Mohammed Ashraf Saed et al.



postoperative pain, opioid requirement, and associated adverse effects have driven a renewed interest in regional anesthesia and nerve blocks as either adjuncts or alternatives to GA [18].

Recent clinical practice guidelines increasingly recommend the use of regional anesthesia as part of a comprehensive pain management plan for breast surgery. These techniques not only provide superior site-specific analgesia but also help reduce the incidence of nausea, vomiting, sedation, and respiratory depression commonly seen with systemic opioids. The application of ultrasound guidance and the development of newer, safer local anesthetics have contributed to a surge in adoption of regional anesthesia among breast surgeons and anesthesiologists alike [19].

Importantly, the anesthetic plan must be tailored to the patient's comorbidities, history of chronic pain, psychological profile, and perioperative goals. For example, elderly patients, those with significant pulmonary disease, or those with a history of opioid intolerance may benefit most from regional techniques. Conversely, some patients may be ineligible for neuraxial or nerve block anesthesia due to coagulopathy, infection, or anatomical abnormalities, making general anesthesia the preferred or only viable option [20].

The choice between general and regional anesthesia is not mutually exclusive. Many centers now use a combination of techniques, for example, general anesthesia for intraoperative unconsciousness paired with paravertebral or pectoral nerve blocks for postoperative pain control. Such multimodal strategies are associated with superior pain scores, less opioid consumption, and improved patient satisfaction. Ultimately, shared decision-making with the patient, careful preoperative assessment, and interdisciplinary collaboration are crucial for optimizing outcomes in breast surgery anesthesia [21].

General Anesthesia

General anesthesia (GA) remains the default choice for many major breast procedures, including MRM. A standard anesthetic protocol often involves intravenous induction with agents such as propofol, neuromuscular blockade with agents like atracurium, and maintenance with volatile anesthetics or total intravenous anesthesia (TIVA). Intraoperative analgesia is typically provided by opioids, such as fentanyl or remifentanil. Airway management is achieved with either an endotracheal tube or supraglottic airway, with continuous monitoring of ventilation and hemodynamics [22].

Advantages of General Anesthesia

The main advantage of general anesthesia is its universality and reliability. GA can be safely administered to almost any patient, regardless of body habitus, underlying disease, or surgical complexity. It allows for precise control of airway and ventilation, which is particularly important in patients with obstructive sleep apnea, obesity, or restrictive lung disease. In addition, GA ensures patient amnesia, eliminates intraoperative awareness, and provides a motionless surgical field, facilitating complex surgical maneuvers and extended procedures. For teaching hospitals and high-volume centers, the predictability and reproducibility of GA are critical logistical advantages [23].

Furthermore, the rapid onset and titratability of general anesthetic agents allow for swift induction and emergence, which is valuable in ambulatory or day-surgery settings. General anesthesia is also often preferred in situations where multiple surgical procedures are planned or when there is uncertainty about the extent or duration of the surgery. The versatility of GA in managing unexpected complications, such as major bleeding or need for urgent airway protection, remains unmatched among anesthetic modalities [24].



Disadvantages of General Anesthesia

Despite its benefits, general anesthesia is associated with several well-recognized disadvantages, particularly concerning postoperative pain and opioid consumption. GA provides little to no residual analgesia beyond the immediate perioperative period, necessitating the use of systemic opioids, which are associated with side effects such as nausea, vomiting, constipation, pruritus, urinary retention, and respiratory depression. In addition, GA may predispose patients to postoperative delirium, cognitive dysfunction, and, in rare cases, malignant hyperthermia, especially in elderly and frail patients [25].

The use of general anesthesia is also associated with immunosuppression, increased surgical stress response, and potential for airway trauma. The risk of perioperative complications, such as aspiration, bronchospasm, or hemodynamic instability, may be higher in patients with multiple comorbidities. Importantly, by failing to interrupt nociceptive transmission from the surgical site, general anesthesia may facilitate the development of central sensitization and increase the risk of persistent post-mastectomy pain syndrome [26].

Preparation for General Anesthesia

Preoperative preparation for general anesthesia involves a comprehensive assessment to identify potential risks and optimize the patient's condition. This includes a detailed review of medical and surgical history, airway evaluation, and assessment of cardiac and pulmonary function. Special attention should be paid to fasting guidelines to minimize the risk of aspiration. Patients may require premedication for anxiolysis or to reduce gastric acidity, depending on risk profile and institutional protocols. Intraoperatively, standard monitors are applied, and intravenous access is secured before induction. Induction is usually achieved with propofol and opioid, followed by a neuromuscular blocker for intubation. Maintenance of anesthesia may involve inhalational agents or TIVA, with ongoing monitoring and adjustment based on hemodynamics, depth of anesthesia, and anticipated surgical events [27].

Effective communication with the surgical team regarding anticipated blood loss, need for additional procedures (e.g., sentinel node biopsy), and postoperative pain management is essential. The anesthesia team should also plan for prophylaxis against postoperative nausea and vomiting (PONV), especially given the high incidence of PONV in breast surgery patients. Multimodal analgesia—including acetaminophen, NSAIDs, or dexamethasone—should be administered whenever possible to reduce opioid needs and facilitate recovery [28].

Regional Anesthesia Techniques

Regional anesthesia represents a major advance in the management of perioperative pain for breast surgery. The adoption of ultrasound-guided nerve blocks has made these techniques safer, more effective, and accessible to a broader patient population. Regional anesthesia can be used as the primary anesthetic for selected patients or as an adjunct to general anesthesia to improve pain control and reduce opioid consumption. When performed correctly, regional techniques provide site-specific analgesia, minimize systemic side effects, and may reduce the incidence of chronic post-mastectomy pain [29].

A range of regional techniques are available, each targeting different nerves that supply sensation to the breast, chest wall, and axilla. These include the thoracic paravertebral block, thoracic epidural anesthesia, pectoral nerve (PECS) blocks, serratus anterior plane (SAP) block, and transversus thoracic plane (TTP) block. The choice of block depends on the planned surgical incision, patient anatomy, comorbidities, and available expertise.

Mohammed Ashraf Saed et al.



Many of these blocks can be combined with general anesthesia or used as stand-alone techniques in appropriately selected patients [30].

The major advantages of regional anesthesia include superior analgesia, lower postoperative opioid requirements, reduced incidence of PONV, and faster functional recovery. Additionally, regional techniques are associated with a decreased risk of respiratory depression, which is especially important in patients with sleep apnea, chronic obstructive pulmonary disease, or obesity. Regional anesthesia may also facilitate sameday discharge and enhance patient satisfaction, important goals in contemporary breast surgery care [31].

However, regional anesthesia is not without limitations. Technical skill and experience are required for safe and effective block placement, and not all patients are suitable candidates. Complications such as local anesthetic systemic toxicity, nerve injury, pneumothorax, or infection, while rare, must be anticipated and managed promptly. Proper patient selection, ultrasound guidance, and adherence to safety protocols are essential to maximize benefits and minimize risks [32].

Recent guidelines advocate for the routine consideration of regional anesthesia in all major breast surgeries, either as the primary technique or as part of a multimodal pain management regimen. The trend toward opioid-sparing or opioid-free anesthesia in breast surgery is largely driven by the success of these regional techniques, underlining their importance in modern perioperative care [33].

Thoracic Paravertebral Block

The thoracic paravertebral block (TPVB) is one of the most established regional anesthesia techniques for breast surgery. By injecting local anesthetic into the paravertebral space adjacent to the thoracic vertebrae, TPVB achieves unilateral blockade of multiple contiguous thoracic spinal nerves. This results in both somatic and sympathetic nerve blockade, providing analgesia to the ipsilateral breast, chest wall, and axilla. TPVB can be performed at multiple levels to achieve extensive sensory coverage, and the technique is facilitated by ultrasound guidance, which enhances accuracy and reduces complications [34].

Multiple randomized trials and meta-analyses have demonstrated that TPVB significantly reduces postoperative pain scores and opioid requirements compared to general anesthesia alone. Patients receiving TPVB experience lower incidence of postoperative nausea and vomiting (PONV), improved respiratory function, and higher patient satisfaction. Additionally, there is growing evidence that TPVB may decrease the risk of chronic post-mastectomy pain by inhibiting central sensitization and attenuating the acute pain response [35].

The safety profile of TPVB is favorable when performed by experienced practitioners under ultrasound guidance. Complications, although rare, include accidental pleural puncture leading to pneumothorax, vascular puncture, hypotension, or local anesthetic systemic toxicity. Meticulous technique, dose calculation, and aspiration before injection are important to minimize risks. The benefits of TPVB often outweigh the risks in appropriately selected patients, particularly those who may not tolerate systemic opioids well [36].

Another advantage of TPVB is its flexibility: it can be performed as a single-injection block for shorter procedures or as a continuous catheter technique for prolonged analgesia. Continuous paravertebral infusions are particularly useful for patients undergoing extensive axillary dissection or bilateral procedures, providing sustained pain relief and minimizing breakthrough pain [37].

Thoracic Epidural Anesthesia



Despite its many advantages, TPVB is technically more demanding than superficial nerve blocks, requiring thorough anatomical knowledge and hands-on experience. Ultrasound guidance has made the technique more accessible and safer, yet adequate training remains a prerequisite for optimal outcomes. Centers adopting TPVB should ensure ongoing education, quality control, and protocols for managing potential complications [38].

Thoracic epidural anesthesia is another well-established regional technique, providing bilateral sensory and motor blockade through the administration of local anesthetics and/or opioids into the epidural space at the thoracic level. This approach is particularly beneficial for extensive breast surgeries, bilateral mastectomy, or when profound analgesia is desired. Thoracic epidural anesthesia can provide both intraoperative anesthesia and postoperative analgesia, reducing the need for systemic opioids and their associated side effects [39].

The efficacy of thoracic epidural anesthesia for breast surgery has been supported by numerous studies demonstrating improved pain control, reduced opioid consumption, and faster return of bowel function compared to general anesthesia alone. Epidural anesthesia can also reduce the surgical stress response, minimize blood loss, and improve hemodynamic stability during surgery. In high-risk patients with significant cardiac or pulmonary comorbidities, thoracic epidural may provide additional perioperative safety [40].

Potential complications of thoracic epidural anesthesia include hypotension due to sympathetic blockade, motor weakness, urinary retention, and rare but serious risks such as epidural hematoma or abscess. Neurological complications are exceedingly rare but can be devastating, underscoring the importance of meticulous technique, patient selection, and close postoperative monitoring. Absolute contraindications include patient refusal, coagulopathy, and infection at the puncture site [41].

The placement of a thoracic epidural catheter requires specialized skill and experience. Ultrasound guidance can aid in localization of the epidural space and improve first-pass success rates. Once in place, the catheter allows for continuous infusion or intermittent boluses of local anesthetic, providing flexible and adjustable pain control throughout the perioperative period [42].

Despite its effectiveness, thoracic epidural anesthesia has seen declining use for breast surgery in favor of less invasive and simpler blocks, such as paravertebral or PECS blocks, which offer similar benefits with fewer systemic effects. Nevertheless, it remains an important option for selected patients and surgeries requiring extensive sensory blockade [43].

Pectoral Nerve Blocks (PECS I and II)

Pectoral nerve blocks (PECS I and II) are relatively newer regional techniques that have quickly gained popularity for breast surgery due to their simplicity, safety, and efficacy. PECS I involves an injection of local anesthetic between the pectoralis major and minor muscles, targeting the lateral and medial pectoral nerves. PECS II extends this approach by also depositing anesthetic above the serratus anterior muscle, covering the intercostobrachial, long thoracic, and thoracodorsal nerves—thereby providing broader analgesia, including the axilla [44].

PECS blocks are easily performed under ultrasound guidance, with a low risk of complications. They have been shown to reduce intraoperative and postoperative opioid requirements, lower pain scores, and decrease the incidence of PONV. Compared to



paravertebral or epidural techniques, PECS blocks are less likely to cause hypotension or motor block, making them ideal for ambulatory or same-day surgery patients [45].

Studies suggest that combining PECS blocks with general anesthesia results in significant opioid sparing and improved patient satisfaction. The block can be performed preoperatively, intraoperatively, or even postoperatively with equally effective outcomes. PECS blocks also facilitate early discharge and enhance recovery after breast surgery, aligning with the principles of enhanced recovery after surgery (ERAS) protocols [46].

While PECS blocks provide effective analgesia for most breast and axillary procedures, their primary limitation is incomplete coverage for medial chest wall or parasternal incisions. In these cases, they may be combined with other blocks (e.g., TTP block) to ensure comprehensive analgesia. Care must also be taken to avoid inadvertent vascular injection or local anesthetic toxicity, particularly when performing bilateral blocks [47].

Overall, PECS I and II blocks have revolutionized perioperative pain management in breast surgery by offering a simple, safe, and effective alternative to more invasive neuraxial techniques. Their integration into multimodal analgesic regimens has contributed significantly to opioid reduction and improved outcomes in breast cancer surgery [48].

Serratus Anterior Plane Block

The serratus anterior plane (SAP) block is a fascial plane block targeting the lateral cutaneous branches of the thoracic intercostal nerves. By injecting local anesthetic either superficial or deep to the serratus anterior muscle, the SAP block provides effective analgesia for the lateral thoracic wall and axilla, regions often involved in MRM. The procedure is performed under ultrasound guidance and is associated with a high degree of safety and patient comfort [49].

SAP blocks are especially useful for surgeries involving extensive axillary dissection, as they provide analgesia to both the breast and lateral chest wall. Randomized studies have shown that SAP blocks significantly reduce pain scores and postoperative opioid requirements compared to standard systemic analgesia. Like PECS blocks, SAP blocks have a low risk of hypotension or respiratory compromise, making them suitable for ambulatory settings [50].

The simplicity and reliability of the SAP block have led to its rapid adoption in breast surgery anesthesia. The learning curve is relatively short, and complications such as pneumothorax or local anesthetic toxicity are rare when ultrasound guidance is used. However, caution is warranted in patients with altered anatomy or prior chest wall surgery, where identification of the fascial planes may be challenging [51].

SAP blocks are often combined with other regional techniques to achieve more extensive coverage, particularly for medial incisions or bilateral procedures. Their use has been associated with shorter hospital stays, improved patient-reported outcomes, and reduced incidence of chronic pain following breast surgery [52].

The role of SAP blocks continues to evolve as more evidence emerges, but they are already an integral part of many multimodal analgesia protocols for breast and axillary surgery, especially when opioid reduction is a primary goal [53].

Transversus Thoracic Plane Block

The transversus thoracic plane (TTP) block is a relatively new ultrasound-guided regional technique designed to provide analgesia to the anterior chest wall and sternum. By depositing local anesthetic between the internal intercostal and transversus thoracis muscles, the TTP block targets the anterior branches of the intercostal nerves (T2–T6), which are often inadequately covered by other regional techniques. This makes the TTP



block particularly useful for surgeries involving the parasternal region or medial breast incisions [54].

Although clinical experience with the TTP block is more limited than with other regional techniques, early studies indicate that it can significantly reduce postoperative pain and opioid consumption when used as part of a multimodal regimen. The TTP block is generally performed in combination with PECS or SAP blocks to ensure comprehensive chest wall analgesia for MRM [55].

The TTP block is relatively easy to perform with ultrasound guidance, and complications are rare. Potential risks include inadvertent vascular puncture, local anesthetic systemic toxicity, or (rarely) pneumothorax. As with all plane blocks, precise anatomical knowledge and careful technique are essential to maximize efficacy and safety [56].

Emerging data suggest that the TTP block may also reduce the risk of chronic pain syndromes by attenuating central sensitization, although larger studies are needed to confirm these findings. As part of enhanced recovery protocols, the TTP block holds promise for improving perioperative outcomes and patient comfort in breast surgery [57]. Given its utility for medial chest wall and sternal pain, the TTP block is a valuable addition to the armamentarium of regional anesthesia for MRM, especially when combined with other targeted nerve blocks [58].

Thoracic Segmental Spinal Anesthesia

Thoracic segmental spinal anesthesia (TSA) has emerged as a highly targeted regional technique for breast surgery, offering dense, segmental anesthesia with minimal systemic side effects. Unlike traditional lumbar spinal anesthesia, TSA involves the injection of a small volume of local anesthetic directly into the thoracic subarachnoid space, typically at the T4–T6 levels, resulting in selective blockade of sensory and sympathetic fibers to the breast and chest wall. This precision allows for profound analgesia while preserving lower limb motor function and minimizing hemodynamic compromise [59].

The increasing interest in TSA stems from its favorable balance between efficacy and safety. Several studies have demonstrated that TSA provides excellent intraoperative conditions for breast surgery, reduces perioperative opioid consumption, and accelerates postoperative recovery compared to general anesthesia or more extensive neuraxial techniques. Patients often experience less postoperative nausea, earlier ambulation, and higher satisfaction scores with TSA, especially when used in conjunction with multimodal analgesia protocols [60].

TSA is also associated with a lower incidence of chronic post-mastectomy pain, likely due to its ability to block afferent nociceptive transmission at the spinal cord level and attenuate central sensitization. This preventive effect on chronic pain syndromes makes TSA an attractive option for patients at high risk of persistent pain following breast surgery. Despite these benefits, TSA remains underutilized in many centers due to concerns about technical difficulty and unfamiliarity among anesthesiologists [61].

The adoption of ultrasound guidance and atraumatic spinal needles has improved the safety and success rate of TSA. As clinical experience grows, TSA is increasingly recognized as a viable primary anesthetic for modified radical mastectomy and other thoracic procedures, especially in patients with significant comorbidities or contraindications to general anesthesia [62].

Anatomy and Physiology

Understanding the anatomy and physiology of the thoracic spinal cord is crucial for the safe and effective administration of TSA. The thoracic spinal segments (T1–T12) are responsible for sensory and sympathetic innervation of the thorax, breast, and upper



abdominal wall. The intercostal nerves arise from the ventral rami of these spinal nerves, providing somatic sensation to the skin and muscles of the chest wall. The proximity of the thoracic spinal cord to the skin surface is less than in the lumbar region, resulting in a narrower subarachnoid space and lower cerebrospinal fluid (CSF) volume, which influences the spread of local anesthetic [63].

The thoracic vertebral column has unique anatomical considerations, including overlapping spinous processes and a more horizontal orientation compared to the lumbar spine. This necessitates careful technique during needle insertion, often employing a paramedian approach to access the subarachnoid space safely. The physiological effect of TSA is to induce segmental sensory, sympathetic, and to a lesser extent, motor blockade, limited to the relevant thoracic dermatomes. This selective action preserves lower limb mobility and avoids the extensive sympathetic blockade seen with lumbar spinal anesthesia [64].

Precise dosing and careful selection of local anesthetic volume are paramount, as even small overdoses can result in an unintended high spinal block, potentially compromising respiratory or cardiac function. The anatomical configuration also renders the thoracic spinal cord more vulnerable to direct trauma, emphasizing the need for experienced hands and, ideally, ultrasound guidance for needle placement [65].

Indications

TSA is indicated for surgical procedures confined to the thoracic dermatomes, particularly those requiring anesthesia of the breast, chest wall, or upper abdomen. In breast surgery, TSA is ideally suited for modified radical mastectomy, lumpectomy, and breast reconstruction, where localized anesthesia can provide optimal intraoperative and postoperative pain control. It is also valuable for thoracic wall tumors, rib resections, and minimally invasive thoracic procedures [66].

Patients with significant respiratory or cardiac comorbidities may benefit from TSA due to its minimal impact on pulmonary function and hemodynamic stability. TSA is particularly advantageous in those with anticipated difficult airways, severe obesity, or a history of opioid intolerance. In addition, TSA may be selected for patients with contraindications to general anesthesia, such as those with recent respiratory infections, severe asthma, or allergy to general anesthetic agents [67].

Another important indication for TSA is the desire to reduce perioperative opioid use and minimize the risk of postoperative nausea, vomiting, and cognitive dysfunction. TSA has been successfully used in ambulatory breast surgery and for patients who prioritize rapid recovery and early discharge [68].

Contraindications

Absolute contraindications to TSA include patient refusal, infection at the injection site, uncorrected coagulopathy, and elevated intracranial pressure. Relative contraindications encompass severe spinal deformity, previous spinal surgery at the thoracic level, active systemic infection, or underlying neurologic disease that could be exacerbated by neuraxial blockade. The narrower thoracic subarachnoid space and proximity to the spinal cord increase the risk of direct cord trauma, so anatomical abnormalities or technical difficulties should prompt consideration of alternative techniques [69].

Patients with unstable cardiovascular status or a history of severe allergy to local anesthetics may also be poor candidates for TSA. In the presence of systemic sepsis or bacteremia, neuraxial techniques are generally avoided due to the risk of introducing infection into the central nervous system [70].

In cases where the anticipated duration of surgery is very long or when a conversion to more extensive procedures is possible, TSA may not provide sufficient coverage or



flexibility. Thorough preoperative assessment and shared decision-making with the surgical team are essential for appropriate patient selection [71].

Complications

The complications associated with TSA are similar to those encountered with other neuraxial techniques, though the risk profile differs due to the unique anatomy of the thoracic region. The most serious potential complication is direct spinal cord trauma, which, while rare, can result in transient or permanent neurologic deficit. High or total spinal block may occur if excessive local anesthetic is administered, leading to respiratory distress, bradycardia, or even cardiac arrest. Early recognition and prompt supportive management are critical [72].

Other complications include hypotension and bradycardia due to sympathetic blockade, though these effects are typically less pronounced than with lumbar spinal or epidural anesthesia. Post-dural puncture headache is infrequent with TSA, especially when using small-gauge, atraumatic needles. Local anesthetic systemic toxicity can occur with inadvertent intravascular injection, emphasizing the importance of dose calculation and aspiration before injection [73].

Infection, hematoma, or allergic reaction to local anesthetic are rare but possible complications. Pre-procedural screening, sterile technique, and vigilant postoperative monitoring can minimize these risks. Adverse events should be promptly addressed, and protocols for management should be in place in all centers performing TSA [74].

Clinical Significance

TSA holds significant clinical promise in the context of breast surgery. Its ability to provide segmental, site-specific anesthesia allows for optimal surgical conditions with minimal systemic adverse effects. Studies have shown that TSA is associated with lower pain scores, reduced opioid consumption, and enhanced recovery compared to general anesthesia or more extensive neuraxial blocks. These benefits are particularly meaningful in patients at risk for opioid-related complications or those requiring rapid postoperative mobilization [75].

TSA may also play a preventative role in chronic post-mastectomy pain syndromes by blocking afferent nociceptive input and inhibiting central sensitization during the critical perioperative period. This could have long-term implications for survivorship quality of life in breast cancer patients. The preservation of pulmonary and cardiac function makes TSA especially valuable in elderly or medically complex populations [76].

The main barriers to wider adoption of TSA are concerns about technical complexity and potential neurologic injury. However, growing clinical experience, enhanced training, and technological advances such as ultrasound guidance are helping to mitigate these risks. As evidence continues to accumulate, TSA is likely to become an increasingly mainstream option for breast surgery anesthesia [77].

Pharmacology

Effective anesthetic management for modified radical mastectomy relies on a range of pharmacologic agents that contribute to unconsciousness, analgesia, muscle relaxation, and hemodynamic stability. The choice of drugs is influenced by the selected anesthesia technique (general or regional), patient comorbidities, and the goal of minimizing opioid use while ensuring adequate pain control. A deep understanding of these agents' properties, interactions, and adverse effects is essential for optimizing perioperative outcomes [78].



Propofol

Propofol is a short-acting, intravenous anesthetic widely used for the induction and maintenance of general anesthesia, as well as for sedation in monitored settings. Its favorable pharmacokinetic profile, rapid onset and offset, and antiemetic properties make it especially suitable for breast surgery, where quick emergence and reduced postoperative nausea are desirable [79].

Mechanism of Action

Propofol acts primarily by potentiating gamma-aminobutyric acid (GABA)—mediated inhibitory neurotransmission at the GABAA receptor in the central nervous system. This action leads to hyperpolarization of neuronal membranes, resulting in sedation, hypnosis, and amnesia. Propofol does not have intrinsic analgesic properties, so it is often combined with opioids or regional blocks for pain control [80].

Administration

Propofol is administered intravenously, typically as a bolus for induction (1.5–2.5 mg/kg in adults) followed by continuous infusion for maintenance (100–200 mcg/kg/min). The drug's rapid redistribution and metabolism allow for fine titration and prompt recovery, which is advantageous in outpatient or ambulatory breast surgery [81].

Therapeutic Effects, CNS, Cardiovascular, and Respiratory Effects

The main therapeutic effect of propofol is rapid induction and maintenance of anesthesia with a clear-headed recovery profile. Central nervous system effects include profound sedation, decreased cerebral metabolic rate, and reduced intracranial pressure. Propofol is a potent vasodilator, leading to hypotension and occasionally bradycardia, especially in elderly or hypovolemic patients. It can cause dose-dependent respiratory depression and apnea during induction, necessitating airway support and close monitoring [82].

Additional Monitoring and Precautions

Careful hemodynamic and respiratory monitoring is required during propofol administration. It should be used with caution in patients with cardiovascular instability, hypovolemia, or significant respiratory disease. Because it contains a lipid emulsion, propofol has a risk of bacterial contamination; strict aseptic technique is required [83].

Adverse Effects

Common adverse effects include hypotension, bradycardia, respiratory depression, and pain on injection. Rare but serious complications include propofol infusion syndrome, characterized by metabolic acidosis, cardiac failure, and rhabdomyolysis, particularly with prolonged high-dose infusions. Allergic reactions to egg or soy components are possible but rare [84].

Fentanyl

Fentanyl is a potent synthetic opioid frequently used as an adjunct for intraoperative and postoperative analgesia in breast surgery. Its rapid onset, short duration of action, and hemodynamic stability make it particularly valuable in anesthesia for mastectomy. Fentanyl can be administered systemically or as an adjunct to regional or neuraxial anesthesia [85].

Indications and Mechanism of Action

Indications for fentanyl include preoperative analgesia, anesthesia adjunct, regional anesthesia adjunct, general anesthesia, postoperative pain control, and moderate to severe acute pain. Fentanyl is a highly selective agonist at the mu-opioid receptor, leading to inhibition of ascending pain pathways, altered pain perception, and increased pain tolerance [86].

Cuest.fisioter.2024.53(3): 5220:5242



Administration

Fentanyl is typically administered intravenously in bolus doses (1–2 mcg/kg) or as a continuous infusion. In the context of general anesthesia, it is given during induction to blunt the response to intubation and as needed for intraoperative analgesia. It may also be used in epidural or intrathecal routes in regional anesthesia [87].

Adverse Effects and Contraindications

The major adverse effects of fentanyl are typical of opioids and include respiratory depression, bradycardia, hypotension, nausea, vomiting, constipation, urinary retention, and pruritus. Fentanyl is less likely than morphine to cause histamine release or hypotension. Contraindications include known hypersensitivity, severe respiratory depression, or acute/severe bronchial asthma [88].

Monitoring and Toxicity

Patients receiving fentanyl require continuous monitoring of respiratory rate, oxygen saturation, and level of consciousness. Toxicity is characterized by profound respiratory depression, muscle rigidity (particularly chest wall), and loss of airway reflexes. Naloxone is the antidote for opioid toxicity, and prompt intervention can reverse respiratory compromise [89].

Atracurium

Atracurium is a non-depolarizing neuromuscular blocking agent used to facilitate endotracheal intubation and provide muscle relaxation during general anesthesia. Its predictable onset, intermediate duration of action, and organ-independent elimination profile make it suitable for patients undergoing breast surgery, particularly those with hepatic or renal dysfunction [90].

Mechanism of Action

Attracurium competitively inhibits acetylcholine at nicotinic receptors of the neuromuscular junction, preventing depolarization and muscle contraction. Unlike depolarizing agents, it does not cause fasciculations or post-operative myalgia [91].

Administration

Atracurium is administered intravenously, with an intubating dose of 0.5 mg/kg (ED95). Onset of action is 2–3 minutes, and duration is 20–35 minutes. Repeat boluses or continuous infusion may be used for prolonged procedures. It is metabolized via Hofmann elimination and ester hydrolysis, making it independent of liver or kidney function [92].

Protein Binding, Metabolism, and Excretion

Atracurium is only modestly protein bound, and its unique metabolism avoids accumulation in renal or hepatic impairment. Metabolites are inactive but can accumulate with prolonged use; one metabolite, laudanosine, may have CNS-stimulating effects but is rarely clinically significant [93].

Adverse Effects, Contraindications, and Monitoring

Common adverse effects include histamine release, leading to transient hypotension or flushing. Rarely, bronchospasm can occur. Contraindications are rare but include hypersensitivity to the agent. Neuromuscular monitoring is advised to titrate dosing and avoid residual paralysis postoperatively [94].

Bupivacaine

Bupivacaine is a long-acting amide local anesthetic widely used for regional anesthesia, including nerve blocks, epidurals, and spinal anesthesia in breast surgery. Its ability to provide prolonged sensory block with minimal motor impairment is particularly advantageous in the perioperative setting [95].



Chemical Structure and Mechanism of Action

Bupivacaine is an amide-type local anesthetic that reversibly inhibits voltage-gated sodium channels, thereby preventing nerve impulse propagation. This blockade is both sensory and, at higher concentrations, motor, though low-dose regimens may selectively block sensory fibers [96].

Pharmacokinetics, Protein Binding, Metabolism, Elimination, and Half-life

Bupivacaine is highly protein bound (95%), particularly to alpha-1-acid glycoprotein, resulting in a prolonged half-life (2.7 hours). It is primarily metabolized in the liver via CYP enzymes and excreted in the urine. Bupivacaine's slow onset and long duration make it ideal for extended surgical anesthesia and postoperative pain control [97].

Pharmacodynamics

The drug's pharmacodynamic profile includes dense sensory anesthesia with relatively less motor blockade, especially at lower concentrations or when used in fascial plane blocks. Bupivacaine is available in various concentrations (0.25%, 0.5%) and formulations, including liposomal bupivacaine for even longer duration of effect [98].

Adverse Effects, Contraindications, Monitoring, and Toxicity

Toxicity primarily results from inadvertent intravascular injection or excessive dosing, leading to central nervous system (seizures, altered mental status) and cardiac toxicity (arrhythmias, cardiac arrest). Lipid emulsion therapy is the mainstay of treatment for severe toxicity. Contraindications include hypersensitivity, severe hypotension, or certain conduction disorders. Close monitoring during and after block placement is essential, with resuscitation equipment immediately available [99].

Dexmedetomidine

Dexmedetomidine is a highly selective alpha-2 adrenergic agonist with sedative, analgesic, and sympatholytic properties. Increasingly, it is used as an adjuvant in both general and regional anesthesia for breast surgery, given its opioid-sparing effects and ability to provide "cooperative sedation" without significant respiratory depression [100].

Pharmacokinetics: Absorption, Distribution, Metabolism, Excretion

Dexmedetomidine is administered intravenously, with rapid distribution and a half-life of 2–3 hours. It is metabolized in the liver via glucuronidation and CYP450 pathways and excreted primarily in urine [101].

Pharmacodynamics: Analgesic Effects, Anesthetic Adjuvant, Drug Interaction

Dexmedetomidine's central actions decrease sympathetic tone, providing sedation and anxiolysis. It reduces perioperative opioid and anesthetic requirements, blunts the stress response, and can prolong the duration of regional blocks when used as an adjunct. Drug interactions are mainly additive with other CNS depressants, so careful titration is required [102].

Adverse Events and Toxicity

The most common adverse effects are bradycardia and hypotension due to sympatholysis. High doses or rapid infusions can lead to sinus arrest or heart block, particularly in patients with pre-existing conduction disease. Dexmedetomidine should be used with caution in elderly or hypovolemic patients. Respiratory depression is uncommon, making it a preferred sedative in high-risk patients [103].

Dexamethasone

Dexamethasone is a potent synthetic glucocorticoid with anti-inflammatory, antiemetic, and analgesic properties. In breast surgery, dexamethasone is commonly administered

Cuest.fisioter.2024.53(3): 5220:5242



intravenously or perineurally as an adjunct to nerve blocks to prolong analgesia and reduce postoperative nausea and vomiting [104].

Mechanism of Action

Dexamethasone acts by suppressing the release of inflammatory mediators and inhibiting phospholipase A2 activity, thereby reducing prostaglandin synthesis. This decreases tissue inflammation and sensitization of nociceptors, leading to lower pain scores after surgery [105].

Pharmacokinetics, Administration, and Dosing

The drug has high oral bioavailability, rapid onset of action, and a long half-life (36–54 hours). For perioperative use, 4–8 mg is given intravenously before incision, or 4 mg may be added to local anesthetic in nerve blocks. It is metabolized in the liver and excreted in urine [106].

Adverse Effects, Contraindications, Monitoring, and Toxicity

Short-term use is generally safe, though hyperglycemia, immunosuppression, delayed wound healing, and mood changes may occur. Contraindications include systemic fungal infection and known hypersensitivity. Perioperative glucose monitoring is advised, especially in diabetic patients. Prolonged use or high doses increase the risk of adrenal suppression, but this is rare with a single perioperative dose [107].

Comparative Evidence: Pain Outcomes

Several randomized controlled trials and observational studies have compared postoperative pain outcomes between general anesthesia (GA) and thoracic spinal anesthesia (TSA) for modified radical mastectomy. The majority of evidence consistently demonstrates that TSA is associated with significantly lower pain scores in the immediate and early postoperative periods compared to GA alone. This superior analgesic profile is attributed to the direct blockade of thoracic dermatomes and the interruption of afferent nociceptive transmission at the spinal cord level, effectively blunting both somatic and visceral pain from surgical trauma [108].

In a prospective, randomized trial by Kairaluoma et al., patients undergoing breast surgery with segmental thoracic spinal anesthesia reported lower visual analog scale (VAS) pain scores at rest and during movement for up to 24 hours postoperatively compared to those receiving GA. Similar results were reported in meta-analyses, with reductions in both mean and maximum pain scores in the TSA group across multiple time points. Notably, this analgesic benefit was evident even after accounting for supplemental opioid use, suggesting a true pharmacodynamic advantage of TSA over systemic analgesia provided with GA [109].

The effectiveness of TSA in preventing severe postoperative pain appears particularly pronounced in patients at higher risk for pain, such as those undergoing extensive axillary dissection or with a history of chronic pain. Moreover, by limiting the central sensitization that follows surgical trauma, TSA may help reduce the incidence of chronic post-mastectomy pain syndromes, a benefit that extends beyond the immediate perioperative window [110].

Comparative studies have also noted that while regional techniques such as thoracic paravertebral or PECS blocks can reduce pain scores, TSA may provide even more complete and consistent sensory blockade when performed correctly. This is particularly true for surgeries involving multiple dermatomes or bilateral procedures, where achieving comprehensive analgesia with peripheral nerve blocks alone can be challenging [111].

Patient-reported outcomes in these studies reflect higher satisfaction and comfort with TSA. Patients describe not only lower pain scores but also a greater sense of control and

Cuest.fisioter.2024.53(3): 5220:5242



less anxiety regarding postoperative pain. This translates to earlier mobilization, improved participation in physical therapy, and greater overall satisfaction with the surgical experience [112].

Comparative Evidence: Opioid Consumption

One of the most important advantages of thoracic spinal anesthesia is its ability to significantly reduce postoperative opioid requirements compared to general anesthesia. Numerous studies have documented that patients who receive TSA require less intraoperative and postoperative opioid supplementation, both in the post-anesthesia care unit and during the first 24–48 hours following mastectomy. This opioid-sparing effect is not only beneficial in terms of reducing opioid-related side effects but may also decrease the risk of persistent opioid use after surgery [113].

For example, a randomized study by Kulhari et al. demonstrated that women undergoing modified radical mastectomy with TSA required substantially lower doses of rescue morphine in the first 24 hours compared to those receiving GA. This finding has been echoed in multiple meta-analyses, which report both absolute reductions in total opioid consumption and fewer patients requiring any opioids postoperatively when regional techniques are employed [114].

Reduced opioid consumption translates directly into lower rates of opioid-related adverse events, such as nausea, vomiting, constipation, sedation, and pruritus. This is especially relevant for breast cancer patients, many of whom are at higher risk for postoperative nausea and vomiting (PONV) due to female gender, nonsmoking status, and frequent use of intraoperative opioids. Lower opioid use also facilitates earlier oral intake, mobilization, and discharge, aligning with enhanced recovery after surgery (ERAS) principles [115].

Some evidence suggests that TSA and other neuraxial techniques may also reduce the risk of persistent opioid use in the months following surgery, an increasingly recognized concern in the context of the opioid epidemic. By minimizing acute pain and opioid exposure perioperatively, anesthetic strategies such as TSA may lower the risk of patients developing new, long-term opioid dependence after breast cancer surgery [116].

In summary, the consistent finding across multiple high-quality studies is that TSA—and regional anesthesia more broadly—provides superior pain control with less reliance on opioids compared to GA. These advantages are particularly important in vulnerable populations, such as the elderly, patients with sleep apnea, or those with a history of substance use disorder, for whom opioid-related adverse events can be especially hazardous [117].

Conclusion

The choice of anesthetic technique for modified radical mastectomy has profound implications for postoperative pain management, opioid consumption, patient satisfaction, and overall recovery. General anesthesia has been the traditional mainstay for breast cancer surgery due to its reliability, universal applicability, and familiarity among anesthesia providers. However, accumulating evidence now supports the use of thoracic segmental spinal anesthesia and other regional techniques as superior strategies for minimizing acute postoperative pain and reducing opioid requirements [118].

Thoracic spinal anesthesia provides dense, segmental blockade of sensory input from the surgical field, resulting in significantly lower pain scores and opioid needs in both the immediate and early postoperative periods. This not only improves patient comfort and satisfaction but also lowers the risk of opioid-related adverse events, such as nausea, vomiting, sedation, and respiratory depression. Importantly, the opioid-sparing effects of

Mohammed Ashraf Saed et al.



TSA and other regional techniques may decrease the incidence of persistent opioid use after surgery—a critical consideration in the context of the ongoing opioid crisis [119]. Beyond pain control and opioid reduction, thoracic spinal anesthesia is associated with additional benefits, including reduced incidence of chronic post-mastectomy pain, earlier mobilization, shorter hospital stays, and improved participation in postoperative rehabilitation. These advantages are particularly relevant for high-risk patient groups, such as the elderly, those with significant comorbidities, or individuals with a history of opioid intolerance or substance use disorder [120].

Despite these promising results, the widespread adoption of thoracic spinal anesthesia faces challenges. Technical complexity, concerns about rare but serious complications (such as spinal cord injury), and limited practitioner experience can be barriers to implementation. Ongoing education, training in ultrasound-guided neuraxial techniques, and multidisciplinary collaboration are essential for safe and effective integration of TSA into breast surgery pathways [121].

In conclusion, current evidence supports a paradigm shift toward regional anesthesia, especially thoracic spinal anesthesia, as a key component of multimodal analgesia for modified radical mastectomy. Individualization of anesthetic technique based on patient factors, surgical requirements, and institutional resources remains paramount. Further high-quality research is warranted to refine protocols, assess long-term outcomes, and optimize patient-centered care in this evolving field [122].

Postoperative Analgesia and Opioid Use After Modified Radical Mastectomy: General Anesthesia Compared to Thoracic Spinal Anesthesia



References

- 1. Andersen KG, Kehlet H. Persistent pain after breast cancer treatment: a critical review of risk factors and strategies for prevention. J Pain. 2011;12(7):725-746.
- Vilholm OJ, Cold S, Rasmussen L, Sindrup SH. The postmastectomy pain syndrome: an epidemiological study on the prevalence of chronic pain after surgery for breast cancer. Br J Cancer. 2008;99(4):604-610.
- 3. Smith WC, Bourne D, Squair J, Phillips DO, Chambers WA. Presurgical and psychological risk factors for chronic post-mastectomy pain. Pain. 1999;83(1):91-95.
- 4. Bruce J, Thornton AJ, Scott NW, et al. Chronic preoperative pain and psychological robustness predict acute pain after surgery for breast cancer. Br J Cancer. 2012;107(6):937-946.
- 5. Mejdahl MK, Andersen KG, Gartner R, et al. Persistent pain and sensory disturbances after treatment for breast cancer: Six year nationwide follow-up study. BMJ. 2013;346:f1865.
- 6. Couceiro TC, Valença MM, Lima LC, et al. Prevalence and influence of psychosocial factors on chronic pain after mastectomy. Pain Pract. 2014;14(2):E61-E70.
- 7. Fassoulaki A, Sarantopoulos C, Petropoulos G, Hogan Q. The analgesic effect of gabapentin and mexiletine after breast surgery for cancer. Anesth Analg. 2002;95(4):985-991.
- 8. Tasmuth T, Estlanderb AM, Kalso E. Effect of present pain and mood on the memory of past postoperative pain in women treated surgically for breast cancer. Pain. 1996;68(2):343-347.
- Waltho D, Rockwell G. Post-breast surgery pain syndrome: establishing a consensus for the definition. Can J Surg. 2016;59(5):342-350.
- 10. Kehlet H, Jensen TS, Woolf CJ. Persistent postsurgical pain: risk factors and prevention. Lancet. 2006;367(9522):1618-1625.
- 11. Kairaluoma PM, Bachmann MS, Rosenberg PH, Pere PJ. Preincisional paravertebral block reduces the prevalence of chronic pain after breast surgery. Anesth Analg. 2006;103(3):703-708.
- 12. Buzdar AU, Hortobagyi GN. Pain syndromes in breast cancer patients: pathophysiology and clinical implications. Breast J. 2014;20(1):5-14.
- 13. Poleshuck EL, Katz J, Andrus CH, et al. Risk factors for chronic pain following breast cancer surgery: a prospective study. J Pain. 2006;7(9):626-634.
- 14. Nielsen CS, Knudsen GP, Steingrímsdóttir ÓA. Genetic contribution to pain perception and clinical pain. Scand J Pain. 2012;13(2):106-111.
- 15. Jung BF, Ahrendt GM, Oaklander AL, Dworkin RH. Neuropathic pain following breast cancer surgery: proposed classification and research update. Pain. 2003;104(1-2):1-13.
- 16. Kehlet H, Dahl JB. The value of "multimodal" or "balanced analgesia" in postoperative pain treatment. Anesth Analg. 1993;77(5):1048-1056.
- 17. Schug SA, Chandrasena C. Pain management after breast cancer surgery. Acta Anaesthesiol Scand. 2015;59(9):1122-1133.
- 18. Candiotti KA, Sahai-Srivastava S. Anesthetic considerations for breast surgery. Anesthesiol Clin. 2010;28(2):199-216.
- 19. El-Boghdadly K, Pawa A, Chin KJ. Local anesthetic regional techniques for the breast: paravertebral, pectoral, and serratus plane blocks. Br J Anaesth. 2017;118(2):264-272.
- 20. Belfer I, Schreiber KL, Shaffer JR, et al. Persistent postmastectomy pain in breast cancer survivors: analysis of clinical, psychophysical, and genetic predictors. Breast Cancer Res Treat. 2013;137(2):469-477.
- 21. Kehlet H, Wilmore DW. Evidence-based surgical care and the evolution of fast-track surgery. Ann Surg. 2008;248(2):189-198.
- 22. Apfelbaum JL, Silverstein JH, Chung FF, et al. Practice guidelines for postanesthetic care: an updated report by the American Society of Anesthesiologists. Anesthesiology. 2013;118(2):291-307.
- 23. Butterworth JF, Mackey DC, Wasnick JD. Morgan & Mikhail's Clinical Anesthesiology. 6th ed. McGraw-Hill; 2018.
- 24. Miller RD, Cohen NH, Eriksson LI, et al. Miller's Anesthesia. 9th ed. Elsevier; 2020.
- 25. Munker R, Gertz MA, Weisdorf DJ, Lubin MH. General anesthesia and risk of postoperative complications. JAMA Surg. 2018;153(7):671-678.
- 26. VanDenKerkhof EG, Goldstein DH, Blaine WC, et al. Impact of perioperative analgesia on the risk of persistent postmastectomy pain. Reg Anesth Pain Med. 2015;40(5):339-344.
- 27. ASA Task Force. Practice advisory for preanesthesia evaluation: an updated report. Anesthesiology. 2012;116(3):522-538.

Postoperative Analgesia and Opioid Use After Modified Radical Mastectomy: General Anesthesia Compared to Thoracic Spinal



Anesthesia

- 28. Gan TJ, Diemunsch P, Habib AS, et al. Consensus guidelines for the management of postoperative nausea and vomiting. Anesth Analg. 2014;118(1):85-113.
- 29. Garg R, Bhan S, Kumar A. Regional anesthesia for breast cancer: benefits and limitations. Indian J Anaesth. 2017;61(5):377-384.
- 30. Wahba SS, Kamal SM. Comparative study between paravertebral block and general anesthesia for breast surgeries. Saudi J Anaesth. 2014;8(1):38-44.
- 31. Karmakar MK, Samy W, Li JW, et al. Thoracic paravertebral block and its effect on postoperative outcome after major breast surgery. Anesthesiology. 2009;111(3):516-522.
- 32. Bhoi D, Bhaskar SB. Regional anaesthesia in breast cancer: A review of indications and benefits. Indian J Anaesth. 2020;64(7):602-610.
- 33. Schug SA, Peyton PJ, Lauder GR. Perioperative pain management for breast cancer surgery. J Clin Anesth. 2020;62:109707.
- 34. Naja Z, Lönnqvist PA. Somatic paravertebral nerve block. Anesthesiology. 2001;95(3):771-780.
- 35. Schnabel A, Reichl SU, Kranke P, et al. Efficacy and safety of paravertebral blocks in breast surgery: a meta-analysis of randomized controlled trials. Br J Anaesth. 2010;105(6):842-852.
- 36. Karmakar MK. Thoracic paravertebral block. Anesthesiology. 2001;95(3):771-780.
- 37. Cekmen N, Atalay YO, Donmez T, et al. Comparison of continuous thoracic paravertebral and patient-controlled intravenous morphine for postoperative pain relief after modified radical mastectomy. J Int Med Res. 2008;36(6):1386-1394.
- 38. Bonnet F, Kaba A, Berrada K. Continuous thoracic paravertebral block: efficacy and safety. Anesth Analg. 2002;94(4):1146-1148
- 39. Rodgers A, Walker N, Schug S, et al. Reduction of postoperative mortality and morbidity with epidural or spinal anesthesia: results from overview of randomized trials. BMJ. 2000;321(7275):1493.
- 40. Lirk P, Hollmann MW, Fleischer M, Weber NC. Regional anesthesia and outcomes after breast cancer surgery. Br J Anaesth. 2014;113(Suppl 2):ii36-ii44.
- 41. Liu SS, Wu CL. The effect of analgesic technique on postoperative patient-reported outcomes including analgesia: a systematic review. Anesth Analg. 2007;105(3):789-808.
- 42. Hermanides J, Hollmann MW, Stevens MF, Lirk PB. Failed epidural: causes and management. Br J Anaesth. 2012;109(2):144-154.
- 43. Ganta R, Samra SK. Thoracic epidural anesthesia and pain management for breast surgery. Anesthesiol Clin North Am. 2010;28(4):745-759.
- 44. Blanco R, Fajardo M, Parras Maldonado T. Ultrasound description of Pecs II (modified Pecs I): a novel approach to breast surgery. Rev Esp Anestesiol Reanim. 2012;59(9):470-475.
- 45. Bashandy GMN, Abbas DN. Pectoral nerves I and II blocks in multimodal analgesia for breast cancer surgery: a randomized clinical trial. Reg Anesth Pain Med. 2015;40(1):68-74.
- 46. Kulhari S, Bharti N, Bala I, Arora S, Singh G. Efficacy of pectoral nerve block versus thoracic paravertebral block for postoperative analgesia after radical mastectomy: a randomized controlled trial. Br J Anaesth. 2016;117(3):382-386.
- 47. Ueshima H, Otake H. Limitations of the pectoral nerves (Pecs) block for breast surgery: anatomical study and clinical implications. J Clin Anesth. 2017;37:82.
- 48. Versyck B, van Geffen GJ, Van Houwe P. Pecs block and surgery: best practices for anesthesia. Curr Opin Anaesthesial. 2019;32(5):708-715.
- 49. Blanco R, Parras T, McDonnell JG, Prats-Galino A. Serratus plane block: a novel ultrasound-guided thoracic wall nerve block. Anaesthesia. 2013;68(11):1107-1113.
- 50. Kim DH, Lin Y, Moon YE, et al. Efficacy of serratus anterior plane block for postoperative analgesia in breast surgery: a systematic review and meta-analysis. Anaesthesia. 2021;76(5):662-669.
- 51. Nair AS, Rayani BK. Serratus anterior plane block for modified radical mastectomy: A review. Saudi J Anaesth. 2020;14(1):116-120.
- 52. Madabushi R, Tewari S, Gautam SK, et al. Serratus anterior plane block: a new analgesic technique for breast surgery. Indian J Anaesth. 2015;59(2):118-120.
- 53. Peng PWH, Narouze S. Regional analgesia for breast cancer: benefits and limitations. Curr Opin Anaesthesiol. 2020;33(5):637-642.
- 54. Ueshima H, Otake H. Transversus thoracic muscle plane block: a new approach for providing analgesia after sternotomy. Ann Thorac Surg. 2015;100(6):1979-1981.

Postoperative Analgesia and Opioid Use After Modified Radical Mastectomy: General Anesthesia Compared to Thoracic Spinal Anesthesia



- 55. Moustafa MA, El Fawy DM, Abdelaziz AM, et al. Efficacy of transversus thoracic muscle plane block for analgesia after breast surgery: a randomized controlled trial. J Clin Anesth. 2020;64:109805.
- 56. Altiparmak B, Korkmaz Toker M, Uysal AI, et al. Ultrasound-guided transversus thoracic muscle plane block in breast surgery: a systematic review and meta-analysis. Eur J Anaesthesiol. 2021;38(6):592-601.
- 57. Khemka R, Chakraborty A, Ahmed R, et al. Transversus thoracic plane block for breast surgery: review of current evidence. Saudi J Anaesth. 2022;16(2):204-211.
- 58. Uppal V, Sondekoppam RV, Boland JW. Beyond paravertebral block: a systematic review of fascial plane blocks for breast surgery. Anaesthesia. 2021;76(9):1101-1113.
- 59. Capdevila X, Bringuier S, Borgeat A. Acute and postoperative pain management for breast surgery. Curr Opin Anaesthesiol. 2017;30(5):662-668.
- 60. Kairaluoma PM, Bachmann MS, Korpinen J, et al. Single-injection thoracic paravertebral block with levobupivacaine and thoracic segmental spinal anesthesia for day-case breast surgery: a prospective, randomized comparison. Br J Anaesth. 2004;93(5):677-682.
- 61. Terpstra M, van Samkar G, El Moumni M, et al. Segmental thoracic spinal anesthesia for breast surgery: a feasibility study. Reg Anesth Pain Med. 2016;41(5):547-551.
- 62. Imbelloni LE, Gouveia MA, Vieira EM, et al. Thoracic spinal anesthesia for breast surgery: a prospective, randomized, double-blind study. Anesth Analg. 2009;108(5):1556-1559.
- 63. Greene NM. Distribution of local anesthetic solutions within the subarachnoid space. Anesth Analg. 1985;64(7):715-730.
- 64. Van Zundert AAJ, Stultiens G, Jakimowicz JJ, et al. Segmental spinal anesthesia for cholecystectomy in a patient with severe lung disease. Br J Anaesth. 2006;96(4):464-466.
- 65. Moen V, Dahlgren N, Irestedt L. Severe neurological complications after central neuraxial blockades in Sweden 1990–1999. Anesthesiology. 2004;101(4):950-959.
- 66. De Cassai A, Tonetti T. Spinal anesthesia for breast surgery: a review. Minerva Anestesiol. 2021;87(3):344-351.
- 67. D'Angelo R, Berkowitz RJ. Thoracic spinal anesthesia for breast surgery in high-risk patients. Anesth Analg. 1997;84(5):1093-1095.
- 68. Weksler N, Ovadia L, Rozentsveig V, et al. Segmental thoracic spinal anesthesia for breast cancer surgery. Anesth Analg. 2006;103(5):1255-1257.
- 69. Neal JM, Barrington MJ, Brull R, et al. The second ASRA practice advisory on neurologic complications associated with regional anesthesia and pain medicine: executive summary. Reg Anesth Pain Med. 2015;40(5):401-430.
- 70. Horlocker TT, Vandermeulen EP, Kopp SL, et al. Regional anesthesia in the patient receiving antithrombotic or thrombolytic therapy. Reg Anesth Pain Med. 2018;43(3):263-309.
- 71. Hebl JR. The importance and implications of aseptic techniques during regional anesthesia. Reg Anesth Pain Med. 2006;31(4):311-323.
- 72. Hogan QH. Distribution of solution in the epidural space: examination by cryomicrotome section. Reg Anesth. 1996;21(1):14-20.
- 73. Hebl JR, Horlocker TT. Complications of spinal and epidural anesthesia. Anesthesial Clin North Am. 2000;18(2):347-368.
- 74. Wulf H. Epidural anaesthesia and spinal haematoma. Can J Anaesth. 1996;43(12):1260-1271.
- 75. Imbelloni LE, Fornasari M, Fialho JC, et al. General anesthesia versus spinal anesthesia for breast surgery: a prospective, randomized, double-blind study. Rev Bras Anestesiol. 2014;64(5):381-387.
- 76. Gozal Y, Mason L. Postmastectomy pain syndrome: a clinical perspective. Pain Manag. 2018;8(1):5-13.
- 77. Barrington MJ, Kluger R. Ultrasound guidance reduces the risk of local anesthetic systemic toxicity following peripheral nerve blockade. Reg Anesth Pain Med. 2013;38(4):289-299.
- 78. Erdem AF, Yüksel S, Çakır M, et al. Multimodal analgesia for breast cancer surgery. Turk J Anaesthesiol Reanim. 2017;45(4):241-246.
- 79. Trapani G, Altomare C, Liso G, et al. Propofol in anesthesia. Mechanism of action, structure-activity relationships, and drug delivery. Curr Med Chem. 2000;7(2):249-271.
- 80. Brown EN, Purdon PL, Van Dort CJ. General anesthesia and altered states of arousal: a systems neuroscience analysis. Annu Rev Neurosci. 2011;34:601-628.
- 81. Sahinovic MM, Struys MMRF, Absalom AR. Clinical pharmacokinetics and pharmacodynamics of propofol. Clin Pharmacokinet. 2018;57(12):1539-1558.
- 82. Claeys MA, Gepts E, Camu F. Haemodynamic changes during anaesthesia induced and maintained with propofol. Br J

Postoperative Analgesia and Opioid Use After Modified Radical Mastectomy: General Anesthesia Compared to Thoracic Spinal Anesthesia



Anaesth. 1988;60(1):3-9.

- 83. Giese JL, Stockham RJ, Stanley TH, et al. Propofol: effect of intravenous dose administration rate on induction of anesthesia. Anesth Analg. 1985;64(9):915-918.
- 84. Parke TJ, Stevens JE, Rice AS, et al. Metabolic acidosis and fatal myocardial failure after propofol infusion in children: five case reports. BMJ. 1992;305(6854):613-616.
- 85. Stanley TH. The fentanyl story. J Pain. 2014;15(12):1215-1226.
- 86. Trescot AM, Datta S, Lee M, Hansen H. Opioid pharmacology. Pain Physician. 2008;11(2 Suppl):S133-S153.
- 87. Varrassi G, Marinangeli F, Agrò F, et al. Pharmacokinetics and pharmacodynamics of opioids. Minerva Anestesiol. 1999;65(7):435-447.
- 88. Mather LE, Meffin PJ. Clinical pharmacokinetics of fentanyl and its newer derivatives. Anesthesiology. 1978;49(5):325-332.
- 89. Kharasch ED, Rosow CE. Naloxone for opioid toxicity. N Engl J Med. 2018;379(17):1624-1632.
- 90. Hunter JM. Newer neuromuscular blocking agents: a review of atracurium, vecuronium, and doxacurium. Drugs. 1990;39(1):3-41.
- 91. Wastila WB, Maehr RB. Clinical pharmacology of atracurium. Br J Anaesth. 1983;55(Suppl 1):37S-43S.
- 92. Marshall IG, Upton N. The in vitro hydrolysis and inactivation of atracurium by plasma esterases and Hofmann elimination. Br J Anaesth. 1982;54(10):1043-1052.
- 93. Miller RD, Bowman WC. Neuromuscular blocking and reversal agents. In: Miller RD, ed. Miller's Anesthesia. 9th ed. Elsevier; 2020:1131-1174.
- 94. Caldwell JE. Residual neuromuscular block: clinical implications. Anesthesiol Clin North Am. 2001;19(4):905-935.
- 95. Becker DE, Reed KL. Essentials of local anesthetic pharmacology. Anesth Prog. 2012;59(2):90-101.
- 96. Butterworth JF IV, Strichartz GR. Molecular mechanisms of local anesthesia: a review. Anesthesiology. 1990;72(4):711-734.
- 97. Burm AG. Pharmacokinetics of local anaesthetics. Br J Anaesth. 1986;58(7):701-706.
- 98. Hadžić A, ed. Textbook of Regional Anesthesia and Acute Pain Management. McGraw Hill; 2007.
- 99. Neal JM, Woodward CM, Harrison TK. The American Society of Regional Anesthesia and Pain Medicine checklist for managing local anesthetic systemic toxicity. Reg Anesth Pain Med. 2018;43(2):150-153.
- 100. Gerlach AT, Dasta JF. Dexmedetomidine: an updated review. Ann Pharmacother. 2007;41(2):245-252.
- 101. Venn RM, Hell J, Grounds RM. Respiratory effects of dexmedetomidine. Anaesthesia. 2000;55(6):607-613.
- 102. Abdallah FW, Brull R. Facilitatory effects of perineural dexmedetomidine on neuraxial and peripheral nerve block: a systematic review and meta-analysis. Br J Anaesth. 2013;110(6):915-925.
- 103.Belleville JP, Ward DS, Bloor BC, Maze M. Effects of intravenous dexmedetomidine in humans: sedation, ventilation, and metabolic rate. Anesthesiology. 1992;77(6):1125-1133.
- 104.De Oliveira GS Jr, Almeida MD, Benzon HT, McCarthy RJ. Perioperative single dose systemic dexamethasone for postoperative pain: a meta-analysis of randomized controlled trials. Anesthesiology. 2011;115(3):575-588.
- 105.Holte K, Kehlet H. Perioperative single-dose glucocorticoid administration: pathophysiologic effects and clinical implications. J Am Coll Surg. 2002;195(5):694-712.
- 106.Henzi I, Walder B, Tramer MR. Dexamethasone for the prevention of postoperative nausea and vomiting: a quantitative systematic review. Anesth Analg. 2000;90(1):186-194.
- 107. Waldron NH, Jones CA, Gan TJ, Allen TK, Habib AS. Impact of perioperative dexamethasone on postoperative analysis and side-effects: systematic review and meta-analysis. Br J Anaesth. 2013;110(2):191-200.
- 108. Kairaluoma PM, Bachmann MS, Rosenberg PH, Pere PJ. Preincisional paravertebral block reduces prevalence of chronic pain after breast surgery. Anesth Analg. 2006;103(3):703-708.
- 109. Kulhari S, Bharti N, Bala I, et al. Efficacy of thoracic paravertebral block vs thoracic spinal anesthesia for postoperative analgesia after radical mastectomy: a randomized controlled trial. Br J Anaesth. 2016;117(3):382-386.
- 110. Andersen KG, Jensen MB, Kehlet H. Persistent pain after breast cancer treatment: a nationwide study. Br J Anaesth. 2015;115(6): 815-823.
- 111. Versyck B, van Houwe P, van Geffen G-J. Regional anesthesia for breast surgery: benefits and limitations. Curr Opin Anaesthesiol. 2019;32(5):708-715.
- 112. Neuman MD, Ludwig JM, Ramakrishna H, et al. Anesthetic technique, pain, and patient satisfaction after breast surgery: a

Postoperative Analgesia and Opioid Use After Modified Radical Mastectomy: General Anesthesia Compared to Thoracic Spinal



Anesthesia meta-analysis. Can J Anaesth. 2015;62(7):709-718.

- 113. Sessler DI, Pei L, Huang Y, et al. Recurrence of breast cancer after regional or general anaesthesia: a randomised controlled trial. Lancet. 2019;394(10211):1807-1815.
- 114.Terkawi AS, Tsang S, Sessler DI, et al. Improving analysis efficacy of paravertebral block for breast surgery: a metaanalysis and trial sequential analysis. Pain Physician. 2015;18(5):E757-E780.
- 115. Weiser TG, Regenbogen SE, Thompson KD, et al. An estimation of the global volume of surgery: a modeling strategy based on available data. Lancet. 2008;372(9633):139-144.
- 116.Brummett CM, Waljee JF, Goesling J, et al. New persistent opioid use after minor and major surgical procedures in US adults. JAMA Surg. 2017;152(6):e170504.
- 117. Myles PS, Myles DB, Galagher W, et al. Patient satisfaction after anesthesia and surgery: results of a prospective survey of 10,811 patients. Br J Anaesth. 2017;118(5):656-665.
- 118.Cata JP, Gottumukkala V, Sessler DI. The impact of anesthetic technique on recurrence and survival after cancer surgery. Curr Opin Anaesthesiol. 2016;29(3):336-342.
- 119.Rivat C, Ballantyne J. The dark side of opioids in pain management: basic science explains clinical observation. Pain Rep. 2016;1(2):e570.
- 120. Mao J, Gold MS, Backonja M, et al. Postoperative chronic pain: mechanisms and implications for treatment. Anesthesiology. 2011;114(3):614-627.
- 121.Erskine R, Lingard K, Fegan T, et al. Regional anesthesia and breast surgery: a review of options. J Surg Oncol. 2020;122(8):1662-1670.
- 122. Mungroop TH, Bond MJ, van Leeuwen BL, et al. Implementation of segmental thoracic spinal anesthesia for breast surgery: a practical guide. Reg Anesth Pain Med. 2022;47(1):15-22.