

# Improving Patient Outcomes Through State-of-the-Art Pain Control in Breast Cancer Surgery

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## Abstract

Acute postsurgical pain continues to be difficult to manage in patients who undergo breast cancer surgery. Poorly controlled pain can lead to poor patient satisfaction, increased length of stay, and increased risk of opioid adverse events, and may be a factor in the development of chronic pain. A multimodal analgesic regimen that consists of 2 or more nonopioid medications and is initiated in the preoperative phase and continued during the intraoperative and acute postoperative phases may provide the best patient outcomes. These nonopioid medications include, but are not limited to, local anesthetics, acetaminophen, nonsteroidal anti-inflammatory drugs, antiepileptics, alpha-2-adrenergic antagonists, N-methyl-D-aspartate antagonists, and glucocorticoids. This multimodal approach can be a stand-alone protocol or a part of a more comprehensive enhanced recovery after surgery (ERAS) protocol.

**Key words:** multimodal analgesia, acute pain, breast cancer surgery, enhanced recovery after surgery

Postoperative pain control remains a common problem for patients undergoing breast cancer surgery. A recent survey showed that patients' number one concern leading up to surgery is pain.<sup>1</sup> Uncontrolled, acute postoperative pain can lead to an increased surgical stress response. This then has an effect on endocrine, metabolic, inflammatory, and immune functions, which can further stress various organ systems.<sup>2</sup> Appropriate pain control can lead to improved postoperative outcomes as well as decreased pulmonary and cardiac complications.<sup>3,4</sup> In addition, uncontrolled acute postoperative pain is associated with longer stays in the postanesthesia care unit, longer hospital stays, decreased patient satisfaction and quality of life, and increased costs.<sup>5-8</sup> Furthermore, while multifactorial in nature, the incidence of chronic pain may be decreased by an aggressive multimodal approach in the acute postoperative setting.<sup>9,10</sup> As many as 4% to 63% of patients suffer chronic pain after mastectomy,<sup>11-13</sup> and as such, ef-

fective acute pain control remains paramount to patient recovery following breast cancer surgery.

The mainstay of perioperative pain control has been opioids. However, opioids are associated with significant risks and adverse effects (AEs) such as pruritus, constipation, nausea/vomiting, urinary retention, oversedation, and respiratory depression.<sup>14</sup> A recent sentinel event alert by The Joint Commission expressed the need for safe use of opioids in the hospital setting.<sup>15</sup> This alert identified those most at risk for respiratory depression, including patients with obstructive sleep apnea or those who are opioid-naïve or obese, which are common characteristics of patients undergoing breast cancer surgery. Furthermore, opioid abuse is an ever-increasing problem in the United States. A recent survey in 2010 showed that 5.1 million US citizens had used opioids illicitly within the past month.<sup>16</sup> Finding ways to minimize opioids in the treatment of perioperative pain may not only decrease AEs, but also decrease the exposure and subsequent misuse of opioids in society.

A multimodal approach has been used for perioperative pain control in various surgical procedures. Multimodal analgesia is the use of more than 1 class of nonopioid medication to reduce pain and minimize the AEs of any 1 class of pain medication.<sup>17</sup> These medications act via different mechanisms and produce a synergistic effect on acute pain control. A successful multimodal protocol requires coordination between all phases of care: preoperative, intraoperative, and postoperative. Furthermore, the surgical, anesthesia, and nursing teams must all work together to ensure that all aspects of the multimodal plan are followed.

The **Table** lists a sample multimodal approach for breast cancer surgery. A preoperative regimen could consist of an antiepileptic medication, such as gabapentin or pregabalin, acetaminophen, and regional anesthesia. Preemptive analgesia ensures that the medication given is active before and during surgery.<sup>7</sup> This also may decrease afferent transmission of pain signals and decrease acute postoperative pain.<sup>18</sup> Several studies have shown opioid reduction and decreased acute and chronic pain using preemptive antiepileptics such as gabapentin or pregabalin.<sup>19,22</sup> Regional anesthesia for breast cancer surgery could be either paravertebral blocks, pec blocks, or a thoracic epidural injection.<sup>23-29</sup> These

blocks can be either a single-shot block or a continuous infusion via catheter. Several studies have shown decreased postoperative pain when these regional techniques are used for breast surgery. If a transverse rectus abdominis muscle (TRAM) or deep inferior epigastric perforator (DIEP) flap is performed, the use of transversus abdominis plane block (TAP) has also been shown to decrease postoperative opioid use and pain scores.<sup>30</sup>

Intraoperatively, pain control should consist of zero to minimal short-acting opioids and a redose of acetaminophen if adequate time has passed. If the patient didn't receive preoperative regional anesthesia, then the surgeon should perform infiltration with local anesthetics. This can be liposomal bupivacaine, bupivacaine, or ropivacaine, or placement of a continuous wound infiltration catheter.<sup>31-33</sup> The local anesthetic of choice for infiltration should be the one that provides the longest duration of action in order to provide maximal patient benefit. Liposomal bupivacaine, given via single-shot infiltration, may provide more prolonged or extended analgesia postoperatively than standard local anesthetics.<sup>34</sup> Recent data have shown liposomal bupivacaine given via infiltration to be an effective adjunct for postoperative pain control in breast augmentation and reduction.<sup>35</sup> In addition, continuous peripheral or wound catheters can provide several days of pain relief using a continuous infusion of local anesthetic.

The postoperative pain regimen should consist of scheduled acetaminophen, scheduled antiepileptics, scheduled nonsteroidal anti-inflammatory drugs as soon as allowed, and intermittent short-acting opioids. This postoperative regimen should be continued for up to 1 week after surgery. In addition, complementary therapies such as acupuncture, aromatherapy, and healing touch can be offered to the patient. If a continuous catheter is in place, the infusion should consist of, at minimum, a local anesthetic and should be used in the acute postoperative period.

In addition to the medications listed in the preceding paragraphs and the **Table**, several other classes of medications can also be used pending patient selection. Intravenous lidocaine has been used to decrease acute postsurgical pain in many surgical populations.<sup>36,37</sup> N-methyl-D-aspartate (NMDA) antagonists such as ketamine and magnesium may play a role in central sensitization. The alpha-2-adrenergic antagonists clonidine and dexmedetomidine have been used in multimodal approaches in other surgical procedures with success, as they primarily act at the

substantia gelatinosa of the spinal cord. Finally, glucocorticoids such as dexamethasone have been used to minimize inflammation and postoperative pain.

A comprehensive multimodal pain regimen will provide the patient with the most complete pain control. It will minimize opioids, which not only will minimize opioid-related AEs and opioid misuse, but may decrease cancer recurrence.<sup>38</sup> A retrospective study by Exadaktylos et al<sup>39</sup> showed that paravertebral anesthesia and analgesia decreased breast cancer recurrence rates. Prospective studies have shown that paravertebral anesthetics, as opposed to general anesthetic with opioids and inhalation anesthetics, resulted in increased natural killer cell cytotoxicity as well as increased apoptosis in estrogen receptor-negative breast cancer cells.<sup>40,41</sup>

In conclusion, this review of a multimodal approach to acute postsurgical pain can provide a framework for managing patients' pain after breast cancer surgery. This could be used alone or in combination with an enhanced recovery after surgery (ERAS)

**TABLE.** Sample Multimodal Regimen for Breast Cancer Surgery

Preoperative	Intraoperative	Postoperative (up to 1 week after surgery)
Antiepileptic: gabapentin 300 mg-1200 mg OR pregabalin 75 mg-150 mg orally prior to surgery	Minimal short-acting opioids only	Scheduled acetaminophen 1000 mg every 6 hours (maximum dose, 4000 mg/day)
Acetaminophen 1000 mg orally or IV prior to surgery	Redose acetaminophen 1000 mg if 4 hours has passed since last dose	Scheduled antiepileptic: gabapentin (300 mg-1200 mg 3 times daily) OR pregabalin (75 mg 2 times daily)
Regional anesthesia: paravertebral, pec, or thoracic epidural (single-shot or continuous catheter)	Infiltration (if no regional anesthesia was performed) with liposomal bupivacaine, ropivacaine, or bupivacaine OR placement of wound catheters	Scheduled NSAID: ketorolac (15 mg-30 mg IV) OR ibuprofen (600 mg) every 6 hours
		If peripheral or wound catheter is in place, run continuous local anesthetic infusion of either bupivacaine or ropivacaine

IV indicates intravenous; NSAID, nonsteroidal anti-inflammatory drug.

protocol to improve patients' postsurgical outcomes. However, future prospective randomized studies are needed to determine the exact combinations and dosages of multimodal medications to provide the optimal benefit for patients.

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