Patients with breast cancer often require several procedures requiring anesthesia, such as central venous catheter placements, mastectomies, lymph node dissections, and reconstructive surgeries. Recent research findings have suggested there may be a reduced risk of cancer recurrence and chronic pain with specific anesthetic techniques. Regional techniques, total intravenous anesthetics, and select adjuncts have been reviewed to identify their role in breast cancer recurrence and chronic pain. A review of the pathophysiology as it pertains to volatile anesthetics, propofol as a total intravenous anesthetic, paravertebral nerve blocks, dexmedetomidine, and ketorolac, as well as the role each of these plays in the prevention of chronic pain and cancer recurrence is provided. Current research and recommendations for practice are presented in the context of providing anesthesia to mitigate chronic pain and cancer recurrence in patients with breast cancer.

Keywords: Anesthesiology, breast cancer, dexmedetomidine, ketorolac, paravertebral block.

Breast cancer is the most common cancer in women in the United States, with more than 1.1 million new cases reported from 2012 to 2016, according to the Centers for Disease Control and Prevention. These patients often undergo several procedures requiring anesthesia, such as implanted venous access device (Port-A-Cath, Smiths Medical) placement, mastectomy, lymph node dissection, and reconstructive surgery. Given the frequency that these patients undergo anesthesia, it bears considering the impact of anesthesia on their treatment and recovery. Recent research has explored the connection between the type of anesthetic and immune function in the perioperative period, which may have implications for recurrence of breast cancer.

Patients with breast cancer also face challenges related to acute and chronic pain. Acute surgical pain and inflammation is well established to be a prerequisite for the development of chronic pain. For patients undergoing mastectomy, the operation is highly dependent on the patient and may be unilateral or bilateral and may include a tissue flap and/or lymph node dissection. Given the extent of surgery required to remove the cancer and reconstruct the breasts, it is common for these patients to experience chronic pain. The prevalence of chronic pain for patients undergoing a mastectomy is 25% and up to 60% for those treated with breast conserving therapy, axillary lymph node dissection, and radiation therapy.

Risk factors for development of persistent postsurgical pain in patients with breast cancer include younger age, axillary lymph node dissection, low level of social support, genetic susceptibility, type of surgery, location of the breast cancer, radiotherapy, chemotherapy, and acute pain after breast cancer surgery. For reference, chronic pain has been estimated at 10% for inguinal herniotomy and 25% to 50% for thoracotomy. Given the prevalence of breast cancer, the high risk of developing chronic pain, and the implications for a substantial number of surgical patients, it is imperative that anesthesia providers are well educated on the most current practice recommendations.

History

- **Anesthesia and Immune Modulation.** Medications used in anesthesia have effects on the immune system and stress hormones, both of which can contribute to immunomodulation in the perioperative period. In cancer patients, this change in immune status has potential to impact outcomes. There are several components to an immune response. Neutrophils, macrophages, natural killer (NK) cells, T lymphocytes, and B lymphocytes all contribute to an immune response, which is necessary both for healing and control of cancer cells in the body. Neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio values are used for evaluation of risk of recurrence in breast cancer. Several studies found NLR values greater than 3 to be associated with adverse outcomes in patients with breast cancer. The stress response also contributes to changes in hormone secretion of corticotropic, cortisol, and prolactin. Even with treatment, patients are still at risk of cancer recurrence. Risk factors include lymph node involvement and tumor size for those undergoing a mastectomy. Those undergoing breast conservation therapy are at higher risk if they...
are younger and the tumor is ductal carcinoma in situ.\textsuperscript{13} It is known that volatile anesthetics have an immunosuppressive effect; specifically, they decrease the number of neutrophils, T lymphocytes, macrophages, and B lymphocytes.\textsuperscript{9,14} Volatile anesthetics also increase cortisol while decreasing cytokine release, phagocytosis, chemotaxis, cytotoxicity, NK cell activity, and proliferation of T lymphocytes.\textsuperscript{9} NK cell activity has been shown to decrease for several days after a volatile anesthetic.\textsuperscript{9} These changes to immune function put patients at increased risk of recurrence of breast cancer. Conversely, studies have shown that propofol suppresses migration and invasion of cancer cells, as well as has an anti-inflammatory effect targeting neutrophil activity.\textsuperscript{10,14,13} With this understanding, it is important to consider the ramifications of anesthetic choices in these patients.

- **Acute and Chronic Pain in Breast Cancer.** Acute pain occurs during the perioperative period regardless of the type of breast cancer surgery performed. The perception of pain is composed of complex interactions from excitatory and inhibitory neurotransmitters, psychological, environmental, and social factors.\textsuperscript{6} Patients are typically educated about pain expected postoperatively; however, it may extend beyond the immediate postoperative period. Historically, patients with a diagnosis of breast cancer received chemotherapy, radiation therapy, and radical mastectomy with sentinel lymph node dissection.\textsuperscript{16} Although procedures to treat breast cancer have become less invasive, overall, chronic pain still remains an issue. The prevalence of chronic pain in patients receiving breast conserving therapy, axillary lymph node dissection, and radiation therapy, which includes peri-clavicular lymph nodes, is 60%.\textsuperscript{3,8,17} These patients, as are those undergoing mastectomy, are at risk of development of postmastectomy pain syndrome, which is a neuropathic pain condition localized in the axilla, medial upper aspect of the arm, breast, and/or chest wall.\textsuperscript{3} As anesthesia providers, it is imperative to implement perioperative interventions that address both acute pain and the potential for chronic pain in these patients.

The pathophysiology of acute pain involves multiple systems and causes (Figure). Peripheral, spinal, and cerebral areas all contribute to the sensation of pain. Initially, damage to peripheral tissue activates primary afferent neurons by a variety of thermal, mechanical, and chemical stimuli.\textsuperscript{6,18} This leads to opening of cation channels in the neuronal membrane, which is conducted along the sensory axon to the dorsal horn of the spinal cord.\textsuperscript{9} From there, it is projected to the brain by direct monosynaptic contact or multiple excitatory or inhibitory neurons.\textsuperscript{6,18}

Endogenous mechanisms have a role in counteracting this sensitization and decreasing the perception of pain through pathways at the peripheral, spinal, and cerebral level described as the “gate control theory of pain.”\textsuperscript{6,18} At the peripheral level, immune cell–derived opioid peptides accumulate in inflamed tissue in response to pro-inflammatory cytokines, chemokines, stress, catecholamines, corticotropin-releasing factor, or bacteria.\textsuperscript{6} The secretion of opioids activates opioid receptors in peripheral tissues, which inhibit the excitability of nociceptors and the release of excitatory neuropeptides, and produce analgesia.\textsuperscript{6} At the spinal cord level, similar inhibition is achieved by the release of opioids, \( \gamma \)-aminobutyric acid (GABA), or glycine from interneurons.\textsuperscript{5,18} These substances activate presynaptic opioid receptors or GABA receptors on the central nociceptor terminal to decrease excitatory transmitter release.\textsuperscript{6} Finally, the brainstem contributes potent descending inhibitory pathways, which are activated through noradrenergic, serotonergic, and opioid systems.\textsuperscript{6}

Acute pain that is inadequately managed can cause persistent nociceptor stimulation, which causes a progressive increase of output in both peripheral and central neurons known as wind-up.\textsuperscript{6,18} This persistent sensitization of peripheral and central neurons can cause transcriptional changes in the expression of genes coding for transmitters, ion channels, receptors, and signaling molecules including cyclooxygenase-2 (COX-2).\textsuperscript{6} Additionally, in the peripheral and central nervous systems physical rearrangement of neuronal circuits occurs through apoptosis, nerve growth, and sprouting.\textsuperscript{6,18} Long term, these changes are responsible for the sustained sensitization in nociceptors and spinal neurons that contributes to the perception of chronic pain.\textsuperscript{5} To counteract this sensitization, gene expression and the production of opioid peptides is up-regulated by spinal interneurons.\textsuperscript{6,18} However, in chronic pain states these mechanisms are overwhelmed, and the delicate balance between excitatory and inhibitory neurotransmitters is disturbed.\textsuperscript{6}

**Chronic pain** is described as dysfunction in one or more of these areas, which renders typical inhibitory mechanisms ineffective.\textsuperscript{18} The International Association for the Study of Pain describes chronic postsurgical pain as “persistent pain, apparent more than two months postoperatively, which has no other root causes such as recurrence of disease, apparent inflammation, etc.”\textsuperscript{3,6,7,18} Chronic pain can have psychogenic, inflammatory, and neuropathic causes, which make treatment challenging.\textsuperscript{3,6,17} Patients with chronic pain may have pain from the primary tumors before intervention, trauma to tissue and nerves during a mastectomy, as well as psychological implications of a breast cancer diagnosis. Therefore, these patients may have components of each pathology.\textsuperscript{3,17,19} Higher postoperative pain scores and analgesia consumption have been found in patients in whom chronic pain develops after breast cancer surgery, suggesting that optimization of acute pain management may decrease development of chronic pain.\textsuperscript{7}

Typically, for breast cancer surgery a standard general anesthetic is used. Induction is done with a narcotic,
Propofol, and a muscle relaxant, with volatile anesthetic gas used for maintenance of anesthesia.\textsuperscript{20-22} Additional narcotic and muscle relaxant are administered as indicated. This technique has provided adequate amnesia and analgesia for the duration of surgery, and additional intravenous and oral pain medications are administered immediately in the postoperative setting as needed.\textsuperscript{20,21} Recently, new research has called into question whether this technique is best practice for patients with cancer.

**Review of Literature**
- **Propofol.** Propofol has shown to suppress migration and invasion of cancer cells, as well as have an anti-inflammatory effect targeting neutrophil activity.\textsuperscript{10,14,15} In a retrospective cohort study published in 2018, propofol used as a total intravenous anesthetic (TIVA) for colon cancer surgery was associated with better overall survival.\textsuperscript{23} After matching for significant differences in baseline characteristics between 2 groups, overall survival for the TIVA group was 86.6\% compared with 56.5\% for a desflurane anesthetic.\textsuperscript{23} The study authors also found a lower incidence of both local recurrence and distant metastasis in the propofol group (5.6\%) at 3.7 years compared with desflurane (9.1\%) at 3.2 years.\textsuperscript{23} Authors of another retrospective study also reported the difference in overall 1-year and 5-year survival rates as 4.7\% and 5.6\% in favor of propofol over a sevoflurane anesthetic in all cancer sites.\textsuperscript{14} However, when adjustments for confounders were made, there was no significant difference between the 2 techniques in overall survival.\textsuperscript{14}

Propofol may also have a role in decreasing the risk of development and the severity of chronic postoperative pain. in a retrospective study, patients who received a sevoflurane anesthetic were reportedly 1.5 times more
likely to have chronic pain 2 to 24 months postoperatively than those who received propofol.\textsuperscript{8,13} When a TIVA with propofol was paired with paravertebral blocks (PVBs), there was a reduction in 6-month chronic neuropathic pain risk: 12.1% in the PVB group compared with 45.3% in the control group when the authors controlled for confounding factors.\textsuperscript{15,17} Although this combination anesthetic may be a useful adjunct, adequate and appropriate pain control in patients with cancer continues to be a challenge both for the patients and providers.

There are additional considerations to implementing a TIVA. A randomized controlled trial investigating the cost-effectiveness of anesthesia found propofol anesthesia with bispectral index (BIS) monitoring was more expensive than using sevoflurane without BIS monitoring.\textsuperscript{24} According to a survey sent to Australian and New Zealand College of Anaesthetists Fellows, 55.5% of respondents described a higher cost associated with a TIVA to be a barrier to its utilization. Additionally, regarding a TIVA, 84.4% of survey respondents found equipment was difficult to access, 91.3% reported a longer setup time, 88.6% reported higher risk of equipment failure, and 88.6% found it to be a more difficult technique.\textsuperscript{25} These barriers could affect implementation of a TIVA in some practices.

• **Regional Nerve Blocks.** Considering the extent of the opioid epidemic, many providers are incorporating opioid-sparing techniques and adjuncts into their practice. Additionally, there is evidence to suggest opioids may potentiate tumor cell survival and angiogenesis, which could lead to metastasis of cancer.\textsuperscript{5,13,26} Regional anesthesia has long-term benefits for patients with cancer by attenuating the surgical stress response, preservation of immune function, and direct antitumor effects of local anesthetics.\textsuperscript{10,26-28} Study findings have shown that treatment with PVB coupled with propofol preserved NK cell function compared with general anesthesia with sevoflurane and opioids.\textsuperscript{5,10,27,29} Use of PVB with breast cancer surgery was also associated with decreased levels of inflammation and growth factors with proliferative or angiogenesis effects.\textsuperscript{27,29} Another study described a difference in 3-year tumor recurrence in patients who received volatile anesthetic with PVB at 6% vs a volatile anesthetic and patient-controlled anesthesia with morphine at 24%.\textsuperscript{30} However, this retrospective study was done through chart reviews, which does not allow for randomization and limits the generalizability of any conclusions.\textsuperscript{10,26-28} Several other studies described trends that could indicate reduced breast cancer recurrence, but the data did not reach statistical significance.\textsuperscript{4,28} The first randomized controlled trial evaluating the long-term effects of thoracic PVB in breast cancer surgery found no difference in recurrence rates at 5 years; however, the authors acknowledged the sample size was insufficient to detect a treatment effect.\textsuperscript{29}

Regional nerve blocks are often cited as an effective alternative for intraoperative and postoperative pain control and may also reduce the development of chronic pain in patients with breast cancer.\textsuperscript{3,13,26,28} Results of several studies show a decrease in intraoperative opioid use and postoperative pain score in patients receiving PVB as part of their anesthetic management.\textsuperscript{21,31,32} Patients who received a PVB had lower pain scores on a visual analog scale at 0, 2, 4, 12 and 24 hours, with significantly prolonged duration of analgesia and less rescue analgesic consumption up to 24 hours compared with patients who received pectoral nerve blocks (types I and II).\textsuperscript{33} More specifically, a randomized controlled trial comparing patients who received a PVB and propofol anesthetic with patients who received sevoflurane and fentanyl anesthetic reported a reduction in pain scores (visual analog pain scale) by 21% and a decrease in fentanyl dose by 62% in patients who received a PVB.\textsuperscript{31}

Because managing acute pain may prevent the development of chronic pain, it is imperative to manage acute surgical pain in patients with breast cancer.\textsuperscript{7,34} A randomized controlled trial looked at chronic pain after radical mastectomy with PVB combined with TIVA general anesthesia vs TIVA general anesthesia alone. The authors found decreased rates of chronic pain symptoms at 3 and 6 months in the PVB group.\textsuperscript{7} Another study comparing chronic neuropathic pain assessment tools found PVB decreased the risk of chronic neuropathic pain at 6 months postoperatively.\textsuperscript{17} A randomized controlled trial evaluating the long-term effects of thoracic PVB in breast cancer surgery found that patients who received a PVB had a 45% to 50% reduction in the incidence and 50% reduction in severity of chronic pain at 3 and 6 months.\textsuperscript{29} Overall, given the low risk and benefit of a regional nerve block, incorporating it into the anesthetic for patients with breast cancer could provide significant benefit. Unfortunately, barriers in practice models may prevent providers from using this technique. A study examining Certified Registered Nurse Anesthetist (CRNA) perspectives and practices about intraoperative alternatives to opioids found barriers may include providers’ individual knowledge of these strategies, their personal experiences with opioid-alternative strategies, and their departmental and institution-level policies.\textsuperscript{35}

• **Dexmedetomidine.** Adjunct medications, such as dexmedetomidine, have also shown promise in addressing chronic pain in patients with breast cancer. Dexmedetomidine when added in preoperative PVB, at a dose of 1 μg/kg, decreased the amount of intravenous pain medication needed and improved the quality and duration of analgesia of the PVB.\textsuperscript{12,36-38} One study reported intraoperative fentanyl requirements for the control group was 77.3 μg vs 54.6 μg in the group with PVB and dexmedetomidine. In the control group, the postoperative total consumption of morphine was 17.4 mg compared
with the PVB and dexmedetomidine group, which was 2.4 mg.³⁷ Dexmedetomidine also shows benefit as an infusion. In a study published in 2012, researchers evaluated a perioperative infusion of dexmedetomidine (2 μg/mL) of 0.5 mL/kg bolus initiated before induction followed by an infusion of 0.25 mL/kg/h until the completion of surgery then decreased to 0.1 mL/kg/h and continued for up to 24 hours.³⁹ They found this protocol decreased pain scores and analgesia requirements in the first 72 hours as well as decreased severity of chronic pain 3 months after breast cancer surgery.³⁹ Another study demonstrated decreased postoperative consumption of morphine when dexmedetomidine was given at the same dose as part of a TIVA.⁴⁰

Although possibly beneficial to patients, dexmedetomidine may carry some risks for patients with cancer. As an α₂ agonist, dexmedetomidine has been shown to activate α₂-adrenoceptors found in human breast cancer cells, and enhance cell proliferation.²,⁴¹ In animal models, dexmedetomidine has been found to increase metastasis in mice and rat models after only a single exposure.⁴² It is hypothesized that dexmedetomidine may have effects on vascular dilation and constriction, alteration in the expression of epithelial adhesion molecules, and increased capillary permeability to circulating tumor cells.⁴² Another study in animal models reported dexmedetomidine had an effect on the migration of colorectal cancer cells, but results did not reach statistical significance.⁴³ Although this has not been seen with in vivo experiments in humans or in large retrospective studies, several randomized controlled trials are ongoing to explore this potential risk.⁵,⁴⁴,⁴⁵ Therefore, dexmedetomidine should be used with caution in patients with cancer until additional research is conducted.

- **Ketorolac.** Another medication that has shown additional benefit in patients with breast cancer is ketorolac. As previously discussed, the development of chronic pain is closely associated with the inflammatory process. Persistent sensitization of peripheral and central neurons can cause transcriptional changes in the expression of genes coding for transmitters, ion channels, receptors, and signaling molecules including COX-2.⁶ Ketorolac works by inhibiting the enzymes that catalyze the synthesis of prostaglandins and thromboxanes. These substances sensitize nociceptors in the periphery and block glycineergic neuronal inhibition, which enhances excitatory amino acid release at the spinal level.⁶ The result is decreased sen-

### Table 1. Perioperative Interventions and Their Immunomodulatory Effects

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Immune modulation</th>
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<tbody>
<tr>
<td>Surgical stress</td>
<td>• ↑ cortisol, prolactin, and corticotropin</td>
</tr>
<tr>
<td>Volatile anesthetic</td>
<td>• ↑ cortisol</td>
</tr>
<tr>
<td></td>
<td>• ↓ neutrophils, T lymphocytes (number and proliferation), macrophages, and B lymphocytes</td>
</tr>
<tr>
<td></td>
<td>• ↓ cytokine release</td>
</tr>
<tr>
<td></td>
<td>• ↓ phagocytosis, chemotaxis, and cytotoxicity</td>
</tr>
<tr>
<td></td>
<td>• ↓ NK cell activity</td>
</tr>
<tr>
<td>Opioids</td>
<td>• ↑ tumor cell survival</td>
</tr>
<tr>
<td></td>
<td>• ↑ angiogenesis</td>
</tr>
<tr>
<td>Propofol TIVA</td>
<td>• ↓ migration and invasion of cancer cells</td>
</tr>
<tr>
<td></td>
<td>• Anti-inflammatory to neutrophil activity</td>
</tr>
<tr>
<td>Paravertebral nerve block</td>
<td>• ↓ surgical stress response and levels of inflammation</td>
</tr>
<tr>
<td></td>
<td>• ↓ growth factors with proliferative or angiogenesis effects</td>
</tr>
<tr>
<td></td>
<td>• Preservation of immune function</td>
</tr>
<tr>
<td></td>
<td>• Direct antitumor effects of local anesthetics</td>
</tr>
<tr>
<td>Dexmedetomidine</td>
<td>• Activation of α₂ receptors in breast cancer cells, leading to ↑ cancer cell proliferation</td>
</tr>
<tr>
<td></td>
<td>May also:</td>
</tr>
<tr>
<td></td>
<td>• Affect vascular dilation and constriction</td>
</tr>
<tr>
<td></td>
<td>• Alter expression of epithelial adhesion molecules</td>
</tr>
<tr>
<td></td>
<td>• ↑ capillary permeability to circulating tumor cells</td>
</tr>
<tr>
<td>Ketorolac</td>
<td>• Inhibition of enzymes that catalyze synthesis of prostaglandins and thromboxanes, leading to ↓ sensitization of peripheral sensory neurons</td>
</tr>
<tr>
<td></td>
<td>• Attenuation of pain sensation at spinal cord</td>
</tr>
<tr>
<td></td>
<td>• Inhibition of components in pain pathway to prevent “wind-up”</td>
</tr>
</tbody>
</table>

Abbreviations: NK, natural killer; TIVA, total intravenous anesthetic; ↑, increased; ↓, decreased.

⁸References 2, 5, 6, 9, 10, 12, 14, 15, 26-29, 41, and 42
sitation of peripheral sensory neurons and attenuation of pain sensation at the spinal cord. Ketorolac inhibits key components in the pain pathway to prevent "wind-up." It has been used to combat both acute and chronic pain; however, its side effect profile limits long-term use.

Inflammation has long been known to play a major role in cancer pathophysiology. The authors of a study done in animal models found decreased tumor development and reduced invasiveness in mice with mammary tumors treated with R-ketorolac, an enantiomer of ketorolac. Another recent animal study found ketorolac given preoperatively, not postoperatively, eliminated micrometastases in multiple tumor-resection models. The authors described that with preoperative suppression of systemic inflammation or stimulation of inflammation resolution via T-cell immunity, there is potent antitumor activity. In retrospective studies, when ketorolac was given preoperatively, there was a fivefold reduction in recurrence in the 9 to 18 months after breast cancer surgery. However, a recent randomized controlled trial found that a single dose of 30 mg of ketorolac preoperatively did not increase disease-free survival for high-risk patients who met one of the following criteria: an NLR of 4 or greater, node-positive disease, or a triple-negative histology, although lower-risk patients were not evaluated. The authors of another retrospective study found intraoperative administration of 20 to 30 mg of ketorolac was associated with a significant reduction in early metastases in patients with a body mass index greater than 25 kg/m² after unadjusted and adjusted analyses. With little evidence to demonstrate that ketorolac causes clinically significant blood loss and because of the potential benefits it may confer, the use of ketorolac during breast cancer surgery seems appropriate. Table 1 summarizes the immunomodulatory effects of ketorolac and the other perioperative interventions discussed here.

Discussion
Although it is difficult to draw indubitable conclusions from the current state of research, there are trends demonstrating that these interventions may improve patient outcomes with minimal adverse effects. Based on the evidence examined, preoperative placement of regional anesthesia in the form of PVB and dosing of ketorolac, followed by a general anesthetic using a TIVA technique would be ideal for these patients. The benefits of these interventions can be seen in Table 2.

Challenges associated with implementation of these recommendations may be both cost prohibitive and practice related. As mentioned earlier, propofol anesthesia with BIS monitoring is more expensive than a sevoflurane anesthetic. Additionally, a survey of providers found higher cost, longer setup time, higher risk of equipment failure, and difficult technique as barriers to use of a propofol TIVA. There are also challenges to consider when one is incorporating PVBs. Individual CRNAs may have limited knowledge of these strategies, they may have personal experiences from which they prefer opioid techniques, and/or their departmental and institution-level policies may preclude their practice of regional anesthesia. Each of these concerns provides insight into areas for additional investigation to reduce or eliminate these barriers to practice.

Limitations to these recommendations are evident, as most of the published literature citing patient outcomes are retrospective reviews. Although retrospective studies can identify trends, these types of studies are difficult to apply because of an inability to control extraneous variables, randomize groups, and confidently link outcomes to specific treatment. Because breast cancer diagnoses are inherently unique to each patient, as is the course of treatment, it makes generalizing findings particularly difficult. Assembling randomized controlled trials has unique challenges as well. When participating in evaluations of cancer recurrence or chronic pain, patients must maintain contact over an extended period. Attrition is a common problem. Challenges then arise in maintaining the volume of patients required to achieve significance. These are just

<table>
<thead>
<tr>
<th>Anesthetic</th>
<th>Timing of intervention</th>
<th>Benefit</th>
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<tbody>
<tr>
<td>Regional PVB</td>
<td>Preoperative placement of 5 mL of 0.75% ropivacaine into paravertebral space at each level</td>
<td>• Attenuates surgical stress response&lt;br&gt;• Preserves immune function&lt;br&gt;• Achieves direct antitumor effects of local anesthetics&lt;br&gt;• Decreases levels of inflammation and growth factors with proliferative/angiogenesis effects</td>
</tr>
<tr>
<td>Ketorolac</td>
<td>Preoperative dosing of 20-30 mg IV</td>
<td>• Suppresses systemic inflammation&lt;br&gt;• Stimulates resolution of inflammation via T-cell immunity&lt;br&gt;• Has potent antitumor activity&lt;br&gt;• Suppresses migration and invasion of cancer cells&lt;br&gt;• Has anti-inflammatory effect targeting neutrophil activity&lt;br&gt;• Decreases likelihood of chronic pain postoperatively</td>
</tr>
<tr>
<td>Propofol TIVA</td>
<td>Induction and maintenance of anesthesia</td>
<td></td>
</tr>
</tbody>
</table>
a few aspects that demonstrate the challenges of conducting research in the population with breast cancer.

Several studies are currently recruiting to fill some of these gaps in our knowledge base. A clinical trial (NCT02839668) is recruiting patients to investigate the impact of intravenous anesthesia on angiogenesis in patients with breast cancer. The follow-up period is 10 years to determine the rate of cancer recurrence or metastasis among patients with breast cancer undergoing surgical therapy. Another study, NCT03782896, is investigating the link between the perioperative period, acute surgical pain, and chronic pain for patients with breast cancer. These are only a few of the ongoing studies to determine if there is a link between anesthetic choices for these patients and the development of recurrence or metastasis.

**Conclusion**

There is a known link between anesthetic medications, immune function, and inflammatory processes. Given the link from immune function to cancer recurrence and from inflammation to chronic pain, and the prevalence of breast cancer in the surgical population, it is essential that anesthesia providers are knowledgeable about the potential long-term effects of their anesthetics. Although there may be challenges to implementation, ample evidence underlines the importance of anesthetic techniques for patients with breast cancer. Providers may also find that other adjuncts individualized to the patient may optimize the patient’s perioperative course. Additional research is needed into the barriers surrounding implementation of TIVA technique and PVBs, as well as the long-term implications of the immunomodulatory effects of anesthetics.

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Disclosures: None.

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Disclosures: None.

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Contribution: This author made significant contributions to the conception, synthesis, writing, and final editing and approval of the manuscript to justify inclusion as an author.
Disclosures: None.

The authors did not discuss off-label use within the article. Disclosure statements are available for view upon request.