



## Anesthesia Pain and Safety Considerations in Cancer Patients

by Dylan Irvine, BSCh, and Jeffrey Huang, MD

### INTRODUCTION:

The subspecialty of onco-anesthesia has gradually gained traction over the past few years. In addition to the comorbid diseases that some cancer patients present with, the interactions and consequences of their antineoplastic regimens must also be considered when devising an anesthetic plan. These new risks challenge the onco-anesthesia professionals with how to manage their patients safely. Preoperative considerations include the effect of chemotherapeutics on anesthesia administration. Intraoperative considerations include assessing the risks of intraoperative hypothermia in cancer patients, patient positioning and peripheral nerve injury considerations, and monitoring of an anesthetized patient. Postoperative considerations include managing the compound effects of postoperative pain with existing pain from a malignancy, as well as the associations between patient psychological support and postsurgical outcomes.

### PREOPERATION CONSIDERATIONS

#### Effect of Chemotherapeutics on Anesthesia Administration—Cardiac and Pulmonary Considerations

The anesthesia professional must consider a specialized approach to anesthesia administration in patients undergoing chemotherapy treatment who require an elective or emergency

surgery. Two of the most common systems affected by toxicities to chemotherapeutics include the cardiac and pulmonary systems, with the degree of toxicity depending on the specific agents employed, the dosage, and duration of use.<sup>1</sup> Common chemotherapeutics associated with cardiac toxicity include busulfan, cisplatin, cyclophosphamide, doxorubicin, and 5-fluorouracil.<sup>1</sup> For such patients, cardiac and respiratory function should be carefully evaluated prior to the anesthetic to identify the onset and etiology of potential complications. In an emergency situation, the use of Point of Care Ultrasound (PoCUS) can provide anesthesia professionals information regarding volume status, cardiac function, and respiratory function<sup>2</sup> in patients who do not have adequate preoperative assessment.

Patients treated with anthracycline chemotherapy, a family of drugs extracted from *Streptomyces spp.* such as doxorubicin, may develop acute intraoperative left ventricular failure refractory to beta-adrenergic receptor agonists.<sup>1</sup> This acute onset left ventricular failure is likely due to the risk of chemotherapy-induced cardiotoxicity associated with this drug class, which limits their use in some patients.<sup>3</sup> In patients who develop chemotherapy-induced cardiotoxicity, the administration of phosphodiesterase inhibitors are indicated.<sup>1</sup>

Common chemotherapeutics associated with pulmonary toxicity include methotrexate, bleomycin, busulfan, cyclophosphamide, cytarabine, and carmustine.<sup>1</sup> Patients can suffer pulmonary complications, such as dose-dependent interstitial pneumonitis and pulmonary veno-occlusive disease.<sup>1</sup> Initial presentation may be limited to dry cough, breathlessness with exercise, and minimal changes on chest radiograph.<sup>4</sup> However, postoperatively, these patients may require a period of mechanical ventilation.<sup>4</sup> A high concentration of inspired oxygen has been shown to increase the risk of patients developing bleomycin-induced lung injury.<sup>4</sup> Therefore, it has been recommended that reduced intraoperative and postoperative oxygen concentration should be used in patients being treated with bleomycin to reduce the risk of respiratory complications.<sup>4,5</sup>

### INTRAOPERATIVE CONSIDERATIONS

#### Intraoperative Hypothermia in Cancer Patients

Between 50%–70% of all surgical patients will experience intraoperative hypothermia.<sup>6</sup> Surgical duration, age, and baseline body temperature have been identified as risk factors for developing intraoperative hypothermia.<sup>7</sup> Cancer patients undergoing surgical treatment are often subject to increased surgical and anesthesia duration, and therefore may be at increased risk of developing intraoperative hypothermia (core body temperature < 36.0° C during surgery<sup>8</sup>). Intraoperative hypothermia is associated with longer surgical recovery time for general anesthesia, arrhythmias, coagulopathies, longer duration of intubation, and increased postoperative length of hospitalization, compared to normothermic intraoperative patients.<sup>6</sup> Hypothermia during cancer resection has been shown to have significant negative effects on postoperative immune function and cytokine levels, particularly in patients undergoing surgery for gastrointestinal cancer.<sup>6</sup> Cancer patients with intraoperative hypothermia may suffer from an increased incidence of postoperative complications of any types, as well as a higher pathologic state and higher recurrence rate within 12 months, relative to normothermic patients.<sup>8</sup>



## A Multimodal Analgesic Approach for Managing Cancer Patients' Pain is Preferred in the Perioperative Period

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Consequently, for anesthesia duration longer than 60 minutes, intraoperative warming should occur through convective heating using a forced-air warming blanket.<sup>9</sup> Intraoperative infusions or transfusions should be warmed.<sup>9</sup> Postoperatively, patients should be thermally insulated to prevent the development of hypothermia and medications such as clonidine or meperidine can be administered to control shivering.<sup>9</sup> Dexmedetomidine displays similar efficacy to antishivering agents such as clonidine or meperidine, but may increase the risk of sedation, hypotension, dry mouth, and bradycardia.<sup>10</sup>

### Intraoperative Patient Positioning and Peripheral Nerve Injury Prevention

In tumor resection surgeries, nerve injury can often occur because of compression and impingement on neural structures due to tumor tissue. Inappropriate patient positioning can lead to peripheral nerve injury as well. The ulnar nerve, brachial plexus, and common peroneal nerve are the most vulnerable to injury during surgery.<sup>11</sup> Anesthesia professionals should be vigilant during the initial positioning and during the surgery.<sup>11</sup> The use of padded arm boards or padding placed around the elbow has been shown to reduce the risk of upper extremity neuropathy perioperatively.<sup>12</sup> Other padding can be strategically placed to limit the pressure of hard surfaces on the fibular head, which has been used to reduce the risk of peroneal neuropathy.<sup>12</sup>

### Intraoperative Monitoring in an Anesthetized Cancer Patient

Intraoperative monitoring of high-risk patients (high-risk patients are defined by patient history, comorbidities, age, body mass

index, ASA status, frailty, poor mobility, presence of terminal illness, and surgery type and complexity) may allow anesthesia professionals to detect the onset and etiology of shock states earlier so that targeted interventions can be implemented. In hemodynamically stable patients, continuous electrocardiographic monitoring, noninvasive blood pressure measurements, end tidal carbon dioxide monitoring, and peripheral pulse oximetry can be adequate intraoperatively.<sup>2</sup> In hemodynamically unstable patients, an arterial line for continuous invasive blood pressure measurement and arterial blood gas analysis should be considered by anesthesia professionals.<sup>2</sup> Implementation of PoCUS into clinical practice may provide additional information regarding volume status, cardiac function, lung status, and respiratory function, and is emerging as a fundamental approach for earlier detection of intra-abdominal or intrathoracic bleeding or fluid deficiency.<sup>2</sup>

### POSTOPERATION CONSIDERATIONS: The Compound Effect of Postoperative Pain with Existing Pain Due to a Malignancy

The complexity of postoperative pain management for cancer patients is important for anesthesia professionals to consider. Barriers to adequate pain relief among cancer patients may be political (e.g., availability to opioids), prescriber-related (e.g., insufficient education around pain assessment and management, apprehension in prescribing opioids to patients, concerns relating to respiratory depression or excessive sedation), or patient-motivated (e.g., fear of addiction, fear that treatment implies final stages of life, fear of side effects).<sup>13</sup> Pharmacologic management of mild cancer pain often involves nonopioid analgesia such as paracetamol/acetaminophen and/or non-steroi-

dal anti-inflammatory drugs (NSAIDs). Treatment of moderate and severe cancer pain can involve the prescription of “weak,” or less potent opioids and “strong,” or more potent opioids, respectively.<sup>13</sup> In postoperative cancer patients, pain management becomes more complicated due to the potential compounding effect from existing cancer pain, and the pain that can be manifested during the postsurgical period. Persistent postsurgical severe pain has been witnessed in 5–10% of cancer patients, which is often the result of nerve injury followed by central sensitization in response to trauma.<sup>14</sup>

Many cancer patients have been on long-term and high-dose opioids; thus, their opioid requirements throughout the perioperative period will be increased.<sup>15</sup> In these patients, multimodal analgesia strategies are important for providing a baseline of nonopioid analgesia, such as through the administration of paracetamol/NSAIDs and alpha-2-delta subunit modulators such as gabapentin.<sup>15</sup> Perioperative intravenous ketamine reduces postoperative pain medication requirement and pain intensity.<sup>16</sup> In a meta-analysis, it has been shown that the benefits of intraoperative lidocaine infusion to reduce pain are not yet confirmed.<sup>17</sup>

Alternatively, local anesthetic infusion with a long-term catheter placement has been shown to decrease the incidence of chronic pain postoperatively.<sup>18</sup> Peripheral nerve blocks are also utilized for regional anesthesia postoperatively, and the complications, performance time, and local anesthetic requirements have been improved through the application of PoCUS.<sup>18</sup> An advantage of peripheral nerve blocks in managing postoperative pain relative to central neuraxial blocks or general anesthesia is a reduction of systemic side effects such as sympathetic blockage and urinary retention.<sup>18</sup> More recently, the emergence of fascial plane blocks has further expanded the applications of regional anesthesia in terms of managing postoperative pain for conditions involving the thorax and abdomen.<sup>19</sup>

### Patient Psychological Considerations

Psychological distress, in particular, depression, in postoperative cancer patients is an emerging issue in the management of such patients. In these patients, referral and access to psychological support and counseling is important in improving patient outcomes. A study of cancer patients who underwent curative surgical resection for primary lung cancer demonstrates that depression and



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anxiety following surgery were aggravated by the presence of residual symptoms present following surgical intervention.<sup>20</sup> In this study, thoracotomy, postoperative dyspnea, severe pain, and diabetes mellitus were identified as risk factors for postoperative depression, after controlling for the presence of preoperative depression.<sup>20</sup>

Providing access to psychological counseling is important at all stages of cancer treatment.<sup>21</sup> Patients have shown benefit from psychological counseling at all stages of cancer care, from initial diagnosis to treatment and managing long-term functional effects.<sup>21</sup> Psychological distress is also common in breast cancer patients who have undergone mastectomy. Compared to controls, the incidence of depression in patients who underwent mastectomy for breast cancer was significantly increased for up to three years following mastectomy, especially in younger adults.<sup>22</sup> Overcoming and preventing postoperative depression in these patients through psychological counseling may improve morbidity and mortality in these patients.

## CONCLUSION

The challenges faced by onco-anesthesia professionals in safely managing cancer patients perioperatively are diverse and complex. However, proper considerations of the potential risks between anesthesia administration and antineoplastic regimens must be taken to ensure the best quality of care while supporting these vulnerable patients.

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