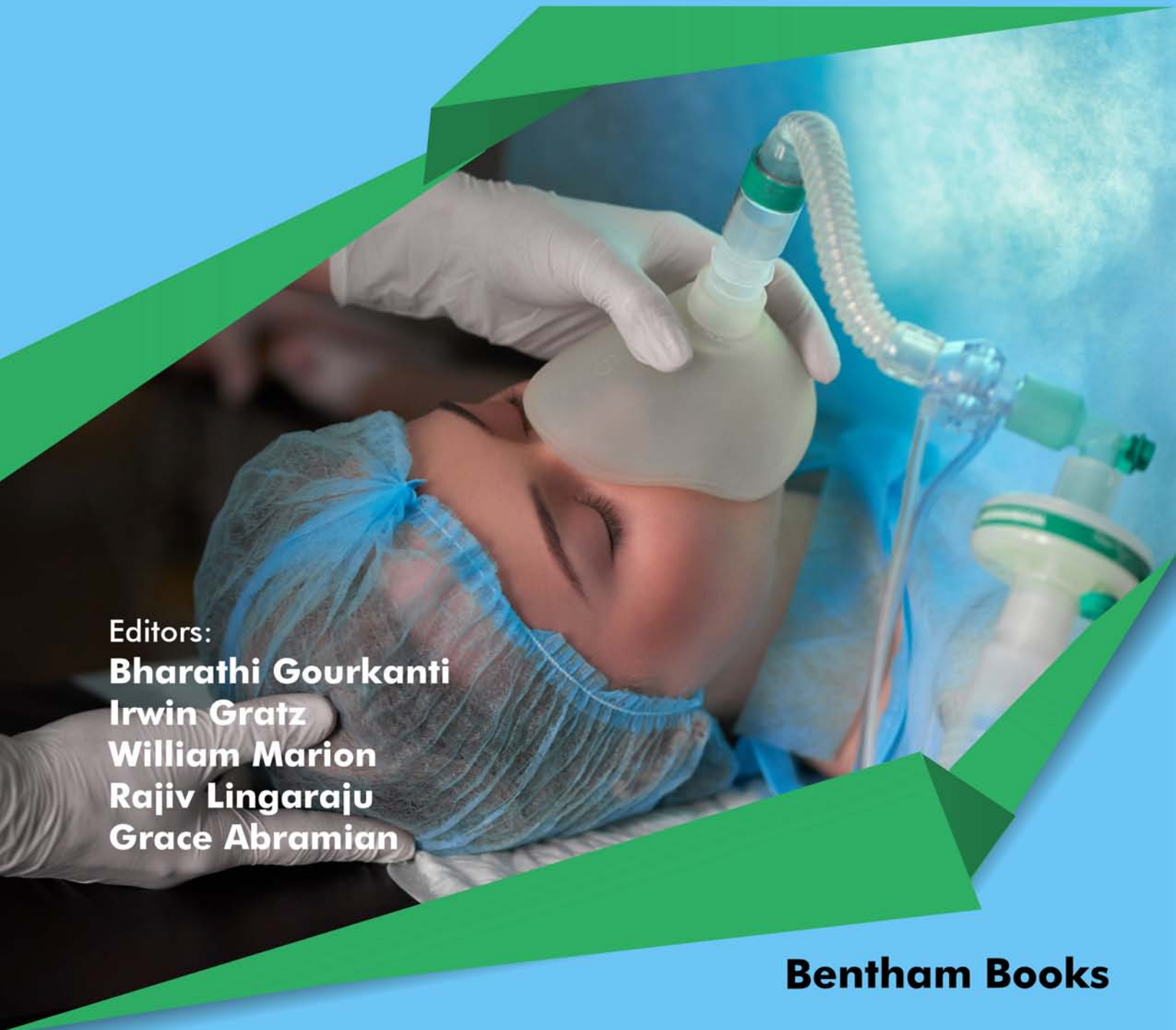
ANESTHESIA CARE FOR CANCER PATIENTS



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Anesthesia Care for Cancer Patients

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FOREWORD

The field of oncoanesthesiology emerged in 2003 with a study investigating the effects of various anesthetic agents on tumor metastasis. Since this study, there have been numerous articles published describing the impact of various anesthetic techniques on natural killer cells, cytokines, T-lymphocytes, and cell apoptosis with the ultimate goal of discovering the preferred anesthetic technique when caring for the patient. This text emphasizes and addresses the importance of the perioperative care of the cancer patient. The anesthesia care these patients require is beyond the knowledge most anesthesia providers gained during their training; the vast body of literature available requires a clear, concise summary. The great news is that both goals are accomplished in this book.

The editors provide an outstanding summary of this emerging specialty, with chapters being written by leading experts. The uniformity in chapter presentation and minimal overlap are a testament to the efforts of the editors to provide a useful book on oncoanesthesiology that will provide new information for both novice and expert anesthesia providers. The inclusion of a chapter on the physiologic changes that occur in a patient with cancer is brilliant and unique. This book is a "must-read" for all who provide anesthesia to patients requiring surgery for cancer. Enjoy the read; You will be glad that you invested your time in reading this book.

Robert Gaiser
Professor of Anesthesiology
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PREFACE

Why this Book?

Having experienced cancer in deeply personal ways—a family member who survived, another who succumbed, and the loss of dear friends—I have been closely involved in the journeys of those affected. Although I have been a practicing anesthesiologist for over 32 years, it had not fully occurred to me how integral anesthesia care is throughout the complex and often tumultuous course of a cancer patient's treatment.

Anesthesia does not cure cancer, but it is required at nearly every stage—from screening and diagnostic procedures to curative and palliative surgeries, as well as pain management. Following these personal experiences, I conducted an extensive literature review and found that while knowledge exists, it is scattered—presented in isolated journal articles, brief topics, or occasional textbook chapters. This realization became my motivation to create a single, comprehensive resource dedicated exclusively to anesthesia care for cancer patients.

Contributors to this Book

To ensure the breadth and depth of expertise, I invited board-certified anesthesiologists representing diverse subspecialties—including general anesthesia, pediatric anesthesia, cardiothoracic anesthesia, pain management, and critical care—to contribute. The team also included anesthesia residents, fellows, researchers, and even a few highly motivated medical students whose curiosity enriched the project. This collective expertise has enabled us to create a resource that we hope will serve as a comprehensive guide to anesthesia care for cancer patients. We believe it will be of value to anesthesia providers, residents, fellows in training, and medical students alike.

Contents of this Book

The book begins with an exploration of the role and importance of anesthesia in cancer treatment, followed by a review of the physiological changes caused by malignancy—knowledge essential for anesthetic planning. We summarize the complications of chemotherapy, radiation therapy, and immunotherapy, along with their anesthetic considerations. The potential effects of anesthesia on tumor metastasis are also discussed. Special chapters address anesthesia care for patients across different age groups with cancer.

We provide detailed guidance on perioperative management—spanning preoperative evaluation through postoperative care—for a wide range of oncologic surgeries, concluding with comprehensive sections on pain management and critical care in oncology.

Acknowledgements

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CHAPTER 1

The Role of Anesthesia in Cancer Management

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Abstract: Cancer affects individuals across all age groups, with epidemiological data indicating a steady rise in the global cancer burden—a trend that closely parallels population growth and aging. As a substantial proportion of cancer patients will require surgical intervention during the course of their disease, this increasing incidence has led to a corresponding surge in demand for cancer-related surgical procedures worldwide. This chapter aims to contextualize the expanding role of oncoanesthesia within the framework of multidisciplinary cancer care, highlighting its influence not only on perioperative outcomes but also on long-term survivorship. To deliver optimal care, healthcare professionals involved in the perioperative management of oncology patients must possess a comprehensive understanding of evolving demographic trends, cancer epidemiology, tumor biology, and the perioperative implications of emerging oncologic therapies. As cancer care continues to evolve, anesthesiologists are increasingly recognized as integral contributors to improving both immediate and long-term outcomes in this growing patient population.

Keywords: Anesthesia, Cancer patients, GI tumors, Immunosuppression, Metastasis, NK cells, Oncoanesthesia, Perioperative management, Regional anesthesia, Total intravenous anesthesia (TIVA), Volatile anesthetics.

INTRODUCTION

Cancer: A Growing Global Health Crisis

Cancer remains one of the most formidable challenges in global public health, contributing significantly to both morbidity and mortality. By 2030, the number of new cancer cases is projected to exceed 22 million annually, underscoring the urgent need for advances in prevention, early detection, and treatment strategies [1]. With a rapidly aging global population and increasing incidence rates, cancer is on track to become the leading cause of death worldwide. Addressing this escalating crisis requires a multifaceted approach integrating research, public

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health initiatives, healthcare policy reform, and specialized clinical care. Currently, cancer is responsible for nearly 10 million deaths annually, accounting for approximately one-sixth of all global deaths [1]. In 2022 alone, an estimated 20 million new cases and 9.7 million cancer-related deaths were reported worldwide [2]. Although cancer comprises a broad spectrum of diseases, a disproportionate burden arises from a few high-incidence malignancies, particularly breast, lung, colorectal, and prostate cancers [2]. Among these, gastrointestinal (GI) cancers, including colorectal, liver, gastric, esophageal, and pancreatic malignancies, are especially lethal, collectively responsible for approximately 34% of all global cancer-related deaths [2].

Despite significant progress in screening, adjuvant therapies, and surgical techniques [3], approximately 20% of patients undergoing curative-intent surgery will experience local or distant recurrence most commonly within the first three years postoperatively, with nearly 80% of recurrences occurring during this critical period [4]. These sobering statistics highlight the urgent need for innovative perioperative strategies to reduce recurrence rates and improve long-term, disease-free survival.

As cancer care becomes increasingly complex, the vast majority of patients will require anesthesia services at some point during their treatment or survivorship journey. This growing demand is further exacerbated by a global shortage of trained anesthesia providers [5, 6]. As cancer incidence continues to rise, the perioperative phase, particularly anesthetic management, has emerged as a crucial component of comprehensive oncologic care.

Global Disparities in Cancer Burden

Disparities in cancer care across the globe are shaped by variations in healthcare infrastructure, the Human Development Index (HDI), environmental exposures, and infection-related risks [2, 7]. High-HDI countries report higher cancer incidence but lower mortality, largely due to greater access to screening, timely diagnosis, and advanced treatments. Conversely, low-HDI countries are experiencing a growing burden in both incidence and mortality, a trend expected to accelerate in the coming decades.

Meanwhile, therapeutic advances, especially in high-income countries, have led to improved survival rates, contributing to a growing population of cancer survivors. These individuals often require anesthesia services for ongoing cancer-related procedures as well as unrelated surgeries throughout survivorship [8].

Anesthesia and Long-Term Cancer Outcomes

One of the most actively investigated areas in perioperative oncology is the potential influence of anesthetic technique on long-term cancer outcomes. While surgery remains the cornerstone of curative treatment for many solid tumors, metastasis is still the leading cause of cancer-related mortality. The perioperative period is characterized by physiological stressors that may inadvertently support tumor cell survival and dissemination. Micrometastases, which may persist or become dislodged during surgery despite optimal techniques, pose a significant risk for recurrence. Additionally, surgical stress can temporarily suppress immune function and trigger pro-inflammatory and pro-angiogenic pathways, creating a perioperative microenvironment conducive to recurrence and metastatic progression [9].

This book explores the connection of the global cancer burden with the evolving role of anesthesia and perioperative medicine. In particular, it examines how anesthetic techniques may influence cancer recurrence and long-term survival. Through this lens, we aim to emphasize the critical and expanding role of anesthesiologists as integral members of the multidisciplinary cancer care team actively contributing to improved oncologic outcomes worldwide.

The Expanding Scope of Oncoanesthesia

Oncoanesthesia, a specialized and increasingly vital field within cancer care, is a critical, yet often underrecognized, component of modern oncologic practice. Its role extends well beyond the administration of anesthesia, encompassing a broad range of perioperative responsibilities, including:

- Prehabilitation and patient optimization
- Advanced perioperative pain management
- Postoperative critical care
- Individualized, multidisciplinary strategies tailored to oncologic comorbidities

As cancer survival rates improve and the number of survivors increases, approximately 80% of cancer patients are expected to undergo one or more surgical procedures during the course of their treatment [2]. These procedures, ranging from curative resections to palliative surgeries, are becoming increasingly complex and often require significant perioperative planning and coordination.

Why Oncoanesthesia Matters

Modern cancer patients frequently present with a range of complex clinical challenges, such as:

CHAPTER 2

Physiological Changes during Malignancy and its Anesthetic Considerations

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Abstract: The perioperative management of cancer patients is complex due to cancer-related physiological alterations and treatment-induced toxicities, requiring tailored anesthetic strategies. Malignancies and therapies like chemotherapy and radiation cause multisystem organ dysfunction, impacting cardiovascular, pulmonary, gastrointestinal, hepatic, renal, and hematologic systems. Surgical stress responses, including catecholamine release and immunosuppression, may promote metastasis. Anesthetic choices, such as total intravenous anesthesia (TIVA) and regional techniques, may mitigate immunosuppression and reduce recurrence risks compared to volatile agents. Preoperative evaluation must address organ-specific toxicities, such as anthracycline-induced cardiotoxicity, bleomycin-associated pulmonary damage, and platinum-based nephrotoxicity. Intraoperative management involves advanced hemodynamic monitoring, lung-protective ventilation, and coagulation management. Postoperative care focuses on early mobilization, multimodal analgesia, and the prevention of complications. Special considerations include tumor lysis syndrome, endocrine paraneoplastic syndromes, and neurotoxicity from chemotherapy. A multidisciplinary approach integrating oncologists, surgeons, and anesthesiologists is essential to optimize outcomes. Prospective studies are needed to validate the impact of anesthetic techniques on long-term oncologic results.

Keywords: Neurotoxicity, Organ dysfunction, Paraneoplastic syndromes, Perioperative management, Pulmonary toxicity, Regional anesthesia, Renal dysfunction, Surgical stress response, Total intravenous anesthesia (TIVA), Tumor lysis syndrome, Volatile anesthetics.

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INTRODUCTION

The perioperative management of cancer patients presents unique challenges for anesthesiologists, stemming from both the pathophysiological alterations induced by malignancies and the complexities introduced by various cancer treatments. A comprehensive understanding of these factors is essential to optimize anesthetic care and improve patient outcomes.

Cancer and its treatments can lead to significant physiological changes affecting multiple organ systems. For instance, certain chemotherapeutic agents are known to cause organ-specific toxicities: bleomycin is associated with pulmonary damage, anthracyclines with cardiotoxicity, and platinum-based compounds with nephrotoxicity. Additionally, many chemotherapy agents can impair liver function and cause gastrointestinal disturbances.

Surgical interventions, while often necessary for cancer treatment, can inadvertently promote tumor metastasis and recurrence. The physiological stress response to surgery, characterized by the release of catecholamines, growth factors, and prostaglandins, may suppress immune function and create a microenvironment conducive to cancer cell dissemination. Local tissue injury during surgery further exacerbates this by inducing inflammation and releasing cytokines, such as interleukin-6 and prostaglandin E_2, which can inhibit natural killer cell activity.

Anesthetic management plays a pivotal role in modulating these perioperative factors. Retrospective data suggest that the choice of anesthetic agents and techniques can influence cancer outcomes. For example, regional anesthesia and the use of total-intravenous anesthesia (TIVA) for general anesthesia have been associated with reduced perioperative immunosuppression, potentially decreasing the risk of cancer recurrence. Conversely, volatile anesthetic agents may have immunosuppressive effects that could promote tumor progression. These are encouraging data that motivate future prospective research to evaluate the potential benefits for cancer recurrence prevention and TIVA-based anesthesia in cancer surgery.

Effective pain management is another critical consideration in the anesthetic care of cancer patients. Uncontrolled pain can lead to chronic pain syndromes and negatively impact the quality of life. Therefore, anesthesiologists must employ multimodal analgesia strategies tailored to the individual patient's needs, balancing effective pain control with minimal side effects.

As an introduction, the anesthetic care of cancer patients requires a nuanced understanding of the disease's impact on physiology, the effects of various

treatments, and the implications of anesthetic choices on cancer progression and patient well-being. A multidisciplinary approach, involving close collaboration with oncologists and surgeons, is essential to navigate these complexities and provide optimal perioperative care [1].

CARDIOVASCULAR CHANGES DURING MALIGNANCY-ASSOCIATED ANESTHETIC CONSIDERATIONS

Cardiovascular Changes Induced by Malignancy

Cancer and its treatments profoundly impact the cardiovascular system, presenting challenges to anesthetic management. Malignancies, directly and indirectly, influence cardiac function through tumor-related cytokine release, paraneoplastic syndromes, and tumor invasion of cardiovascular structures. Additionally, the systemic inflammatory response associated with cancer can exacerbate endothelial dysfunction, pro-coagulant states, and myocardial strain.

Chemotherapy-Induced Cardiotoxicity

Certain chemotherapeutic agents are well-known for their cardiotoxic potential. Anthracyclines, for example, are associated with dose-dependent cardiomyopathy and heart failure due to oxidative stress and mitochondrial dysfunction. Similarly, trastuzumab, a monoclonal antibody targeting HER2, disrupts cardiomyocyte survival pathways, leading to reversible cardiac dysfunction. Platinum-based agents and vascular endothelial growth factor (VEGF) inhibitors contribute to hypertension, ischemia, and left ventricular dysfunction by inducing endothelial damage and impairing nitric oxide production [2 - 4].

The clinical manifestations of cardiotoxicity vary depending on the timing and extent of myocardial injury. Acute toxicity occurs immediately after treatment and manifests as ECG changes, QT prolongation, and various arrhythmias, with rare cases of ventricular fibrillation leading to sudden death. Subacute toxicity may cause acute left ventricular failure, pericarditis, or pericarditis-myocarditis syndrome, particularly in children, while elderly patients with preexisting heart disease may develop transient CHF. Chronic cardiotoxicity, primarily dose-dependent, often leads to cardiomyopathy, cardiomegaly, and progressive CHF, with the risk increasing significantly beyond 550 mg/m^2 of doxorubicin, for instance. Late-onset cardiotoxicity can emerge years after treatment, with previously asymptomatic patients developing heart failure and arrhythmias, potentially due to subclinical myocardial injury that impairs cardiac growth and function over time [2].

CHAPTER 3

Chemotherapy: Complications and Anesthetic Considerations

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Abstract: This chapter explores the relationship between chemotherapy and anesthesia, highlighting the challenges faced in perioperative management of cancer patients. As chemotherapy remains a cornerstone of modern oncologic therapy, its systemic toxicities—including cardiotoxicity, neurotoxicity, hepatotoxicity, nephrotoxicity, and myelosuppression—present unique anesthetic considerations. The chapter systematically reviews major chemotherapeutic drug classes, including alkylating agents, antimetabolites, plant alkaloids, anti-tumor antibiotics, hormonal therapies, and biological response modifiers, alongside their mechanisms, indications, and adverse effects. Common malignancies, such as breast, colorectal, brain, and lung cancers—are discussed in detail to demonstrate how chemotherapy impacts anesthesia choices and perioperative planning. Strategies such as regional anesthesia, preoperative organ function assessment, and individualized anesthetic approaches are emphasized to mitigate risk. The chapter underscores the importance of multidisciplinary collaboration between oncologists, anesthesiologists, and surgeons to optimize outcomes and safety in the evolving field of oncologic surgery.

Keywords: Chemotherapy, Glioblastoma, Lung cancer, Alkylating agents, Anthracyclines, Regional anesthesia, Chemotherapy-induced complications, Anesthetic risk stratification, Oncologic anesthesia.

INTRODUCTION

Cancer is the leading cause of long-term mortality following surgery. Even after a "curative" surgery with complete resection, postoperative cancer returns in up to one-third of patients [1]. As such, many patients who undergo surgery as a means of treating cancer will receive chemotherapy and radiation as indicated to help maximize survival. As cancer care incorporates these multimodal treatment strat-

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egies, understanding the pharmacological and physiological interactions between anesthetic agents and chemotherapeutic drugs has become critically important for optimizing patient outcomes and minimizing perioperative risks.

Chemotherapeutic agents, while essential in managing malignancies, are often associated with systemic toxicities that can significantly influence anesthetic management. For instance, cardiotoxicity from anthracyclines, pulmonary complications from bleomycin, and neurotoxicity from agents like vincristine present unique challenges during anesthesia. Recognizing and anticipating these complications is vital for tailoring perioperative care to individual patient needs.

In addition to direct systemic toxicities, chemotherapy-induced immunosuppression and hematologic disturbances, such as thrombocytopenia and neutropenia, impact preoperative planning and intraoperative vigilance. Perioperative management of the cancer patient mandates a multidisciplinary approach involving oncologists, anesthesiologists, and surgeons to ensure cohesive and informed care. Through case discussions and evidence-based recommendations, the chapter serves as a practical guide for clinicians navigating the perioperative management of cancer patients undergoing anesthesia. Focus on patient safety, individualized care, and interdisciplinary collaboration highlights the evolving demands of modern oncologic anesthesia.

DEFINITIONS

Chemotherapy is described as the use of any drug to target neoplastic cells by targeting mechanisms used by cells that rapidly divide, such as DNA replication, RNA synthesis, and protein synthesis. In doing so, chemotherapeutic drugs can target benign, healthy cells, thereby causing common side effects such as nausea, vomiting, hair loss, diarrhea, fatigue, and easy bruising and bleeding.

The roles of chemotherapy can be curative, palliative, adjuvant, and neoadjuvant. The goal of curative chemotherapy is to achieve complete remission, while the goal of palliative chemotherapy is to relieve symptoms. Adjuvant chemotherapy's goal is to destroy any remaining neoplastic cells and prevent recurrence or relapse. Neoadjuvant chemotherapy is given before surgery or radiation therapy to shrink or prevent the growth of the tumor.

There are numerous types of cancers that respond to chemotherapy, such as leukemias, lymphomas, bone cancer, endometrial cancer, testicular cancer, breast cancer, *etc*., but advanced-stage solid tumors remain more difficult to treat with chemotherapeutic drugs [2]. Solid tumors are difficult to treat with chemotherapy, likely due to a combination of factors, including the presence of a hypoxic and acidic tumor microenvironment and overall tumor heterogeneity.

The overarching strategy of chemotherapeutic agents is to target cell division. Chemotherapies can act in a number of ways, including alkylation, nitrosoureas, antimetabolites, plant alkaloids and natural products, anti-tumor antibiotics, hormonal agents, and biological response modifiers.

MAJOR CLASSES OF CHEMOTHERAPY, COMMON INDICATIONS, SIDE EFFECTS

Alkylating Agents

Alkylating agents are drugs or chemicals that form electrophilic intermediates that bind to the N7 nitrogen of two adjacent guanine nucleotides, causing crosslinking between DNA strands and inhibiting DNA replication or transcription [3]. In the 1940s, these agents were the first non-hormonal drugs to be used in cancer treatment. Nitrogen mustards are commonly used alkylating agents; these agents typically contain a nitrogen group with two chloroethyl groups that act as electrophiles in the alkylation process. SN1 is the first type of alkylating agent [4]. SN1 agents act directly on biological molecules. This is in contrast to SN2 alkylating agents, which create a reactive intermediate. Common alkylating drugs are cyclophosphamide, ifosfamide, chlorambucil, mechlorethamine, and melphalan [3]. Cyclophosphamide is an SN2 alkylating agent that is converted into an active metabolite by cytochrome P450 enzymes and is typically used to treat non-Hodgkin lymphomas, breast, lung, and ovarian cancer. In a randomized trial, a combination treatment of cyclophosphamide, fluorouracil, and epirubicin (CEF) was compared to a combination of cyclophosphamide, methotrexate, and fluorouracil (CMF). Ten-year overall survival rates for CEF and CMF were 62% and 58%, respectively, suggesting a benefit from combination therapies with cyclophosphamide [5]. Ifosfamide is another SN2 agent used to treat sarcomas and testicular cancer. In a meta-analysis, ifosfamide used as preoperative chemotherapy was associated with an increased rate of limb salvage in patients with osteosarcomas of the limbs with an odds ratio of 4.06 ($p<0.001$). Chlorambucil is an SN1 agent used to treat Chronic lymphocytic leukemia or non-Hodgkin lymphoma, while mechlorethamine is an SN1 agent used for Hodgkin and non-Hodgkin lymphoma. In a randomized controlled clinical trial, the event-free survival rate of patients with mucosa-associated lymphoid tissue lymphoma treated with rituximab alone was 50%, but it increased to 68% when combined with chlorambucil [5]. Melphalan is an SN1 primarily used for multiple myeloma, breast, and ovarian cancer. In a randomized clinical trial, melphalan in a drug regimen with bortezomib, daratumumab, and prednisone increased the 18-month progression-free survival of patients with multiple myeloma to 71.6% [6].

CHAPTER 4

Immunotherapy - Anesthetic Considerations

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Abstract: This chapter provides an overview of cancer immunotherapy, tracing its evolution from historical observations to cutting-edge therapies like immune checkpoint inhibitors, CAR T-cell therapy, and bispecific T-cell engagers. We explain how these treatments harness or modify the immune system to target cancer, detailing their mechanisms, clinical applications, and associated toxicities across multiple organ systems. Key agents include CTLA-4 and PD-1/PD-L1 inhibitors, high-dose IL-2, interferons, and therapeutic vaccines like Sipuleucel-T. As these drugs can potentially impact every organ system, thoughtful anesthetic planning for the care of cancer patients is critical for minimizing complications. We emphasize the importance of assessing immune-related adverse events (irAEs) such as pneumonitis, myocarditis, neurotoxicity, and endocrinopathies through preoperative planning and throughout the perioperative period. We advocate for close coordination with oncology and surgical teams to optimize perioperative care. Emerging therapies and future directions—including novel checkpoint inhibitors, CAR-NK cells, and oncolytic viruses—are also discussed, highlighting the field's rapid growth and evolving clinical impact.

Keywords: Anesthetic risk stratification, Bispecific T-cell engagers, BiTEs, Chimeric Antigen Receptor Cells, CAR T-Cells, Immunosuppression, Myasthenia Gravis-like syndrome, Neuropathy, Oncologic anesthesia, Regional anesthesia, Tumor immunology, Vaccines.

INTRODUCTION

History

Cancer immunotherapy is rapidly advancing and has evolved greatly throughout the ages, with anecdotal reports of tumors disappearing after an infection in anci-

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ent Egypt [1]. Busch and Fehleisen were German physicians who noticed the regression of tumors in cancer patients that were unintentionally infected with erysipelas [2]. In 1868, Busch purposefully infected a cancer patient with erysipelas and noted the subsequent shrinkage of the tumor. William Coley, a surgeon in New York, is often cited as the first to attempt immunotherapy. He injected heat-inactivated bacteria called Coley's toxins into patients who were not surgical candidates, noting significant tumor regression [2].

In 1957, the Cancer Immunosurveillance Hypothesis was proposed by Burnet and Thomas, suggesting that the immune system patrols for cancer cells [3]. This eventually formed the basis for tumor immunology and helped explain spontaneous tumor regressions, which guided later research. Shortly after this, the use of Bacillus Calmette-Guerin (BCG), a weakened form of the bacteria that causes tuberculosis, for bladder cancer demonstrated that the resultant immune stimulation could fight tumors [3]. There were several early cytokine therapies, such as interferon-alpha and interleukin-2 (IL-2) that were explored in the 1970s-1980s as cancer treatments. This was an important step that showed evidence of ramping up T-cells to induce remission of cancer. IL-2 is a T-cell growth factor that was FDA-approved for the treatment of metastatic melanoma and renal cell carcinoma in the 1990s [4].

In 1992, Tasuku Honjo identified PD-1 (programmed cell death-1), a protein that acts as a brake on the immune system by regulating T-cell activity [5]. This helped give rise to immune checkpoint inhibitors, which block the interactions between PD-1 and its ligands, allowing the immune system to fight cancer. In 1996, James Allison also contributed to this cause by discovering that CTLA-4 acts similarly as an immune brake, preventing T cells from attacking cancer cells. He developed antibodies to block CTLA-4, allowing T cells to attack tumors. In 2011, Ipilimumab, an immune checkpoint inhibitor, was FDA-approved for the treatment of metastatic melanoma [3]. Combination therapy using anti-CTLA-4 and anti-PD-1 antibodies is often used to improve remission rates. In 2017, the first chimeric antigen receptor (CAR) T-cell therapies were approved for refractory lymphoma [6]. This involves genetically engineering a patient's T cells to express a CAR that recognizes a specific cancer antigen, allowing T cells to target cancer cells.

Current Practice Overview

Immunotherapy has become a mainstay in cancer treatment for a variety of malignancies. Immune checkpoint inhibitors (ICIs) are monoclonal antibodies that block inhibitory receptors like CTLA-4, PD-1, or ligand PD-L1. These are approved for numerous cancers (melanomas, lung cancer, renal cancer,

lymphoma, *etc*). Adoptive cellular therapies, such as CAR T-cell therapy, involve personalized genetic engineering of a patient's T cells to attack tumor cells. T-cell receptor (TCR)- engineered T cells, on the other hand, are engineered to express a modified TCR that recognizes antigens presented on tumor cells by major histocompatibility complex (MHC) molecules. Cytokine therapies, such as high-dose IL-2 and interferon, are older forms of immunotherapy that boost the immune response non-specifically. Cancer vaccines involve exposure to tumor antigens to activate a humoral immune response to tumor-specific antigens [7]. Lastly, bispecific T-cell engagers (BiTEs) are substances that form a bridge by binding T cells with a target antigen on cancer cells, allowing the T cell to destroy the tumor cell [8].

NATIVE ANTITUMOR IMMUNITY

These are the therapies that enhance the body's existing immune response against tumors. "Native" antitumor immunity refers to the immune system's capacity to recognize and destroy cancer cells. Since tumors can evade or suppress this response, the following therapies help overcome this by boosting intrinsic immune functions or removing inhibitory mechanisms.

Immune Checkpoint Inhibitors (ICIs)

ICIs are monoclonal antibodies that block inhibitory receptors or ligands on T-cells and other immune cells, preventing the ability of tumors to evade immune attack.

- ***Mechanism of Action*:** CTLA-4 on T-cells downregulates the immune response by competing with CD28 for binding B7 ligands on antigen-presenting cells. Tumor cells can increase CTLA-4 activity to help prevent T-cell activation. Anti-CTLA-5 antibodies block this inhibition, leading to increased T-cell activation in lymph nodes. PD-1 on T-cells is a "brake" on activated T-cells in peripheral tissues. When PD-1 binds ligand PD-L1 on tumor or immune cells, the T-cell becomes inactive. Anti-PD-1 and anti-PD-L1 antibodies prevent this from happening, allowing T cells to attack tumor cells (Fig. **1**). This enhanced immune activity helps control tumors but also causes autoimmune side effects because of the increased immune activity that has the potential to attack normal organs. Combinations of these different drugs can improve remission at the cost of higher toxicity.
- ***Common Agents and Clinical Use*:** Some examples of anti-CTLA-4 monoclonal antibodies are Ipilimumab and Tremelimumab, though the latter has no clinical indication. Anti-PD-1 monoclonal antibodies include Pembrolizumab and Nivolumab. Lastly, anti-PD-L1 monoclonal antibodies include

CHAPTER 5

Radiation Therapy - Anesthetic Considerations

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Abstract: This chapter will provide an in-depth review of radiation therapy and its implications on anesthetic management. It will begin with a brief overview of cancer and the history of radiation therapy's progression into an essential tool in cancer treatment. Next, the mechanism behind radiation therapy's effectiveness in targeting cancer cells will be explored. Lastly, a systems-based approach to radiation therapy and its impact on anesthetic planning will be discussed.

Keywords: Direct DNA damage, Indirect DNA damage, Ionization, Linear accelerators, Linear energy transfer, Mitotic catastrophe, Radiation therapy, Radiotherapy, Radiation oncology, Radiobiology.

INTRODUCTION

Over the past few decades, cancer treatment modalities have advanced exponentially, driven by large global cancer research and development initiatives. Despite significant advancements in early detection, diagnostic tools, and targeted multimodal therapies, cancer continues to impose a significant burden on healthcare systems worldwide. The International Agency for Research on Cancer (IARC) estimates that there were 20 million new cancer cases with 9.7 million deaths in 2022. By the year 2050, IARC predicts over 35 million new cancer cases yearly, representing a 77% increase from the 20 million cases of 2022 [1]. Given the significant burden of cancer globally, researchers and clinicians must continue to develop and implement these lifesaving advancements in cancer therapies to improve outcomes.

Modern cancer treatment is often tailored specifically to the individual patient based on factors such as comorbidities, age, tumor type, tumor genetics, stage, and location within the body. Although each patient's treatment plan is unique, the overarching principle of therapy remains the same: targeted eradication of

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cancer cells while causing the least amount of damage to surrounding healthy tissues. Currently, cancer treatments can target malignant cells through a variety of modalities. These include radiation therapy, chemotherapy, immunotherapy, and hormonal therapy. Radiation therapy, also called radiotherapy, is one of the oldest and most extensively utilized cancer treatment options available. Its success is evidenced by its use in up to 50% of all cancer treatment plans [2]. The implementation of radiation therapy is utilized in a diverse number of cancer types, including breast, lung, prostate, head and neck, cervix, and brain, among others. Radiation therapy can serve as the primary treatment, in combination with systemic therapy and/or surgery, or in a palliative role to relieve symptoms such as pain and obstructions caused by large tumors. Over the years, its effectiveness and widespread use have led to the establishment of radiation oncology, a medical subspecialty dedicated entirely to the application of radiation therapy.

History of Radiation Therapy

The origins of radiation therapy date back to the revolutionary work of German physicist Wilhelm Roentgen (Fig. **1**). In 1895, while experimenting with cathode ray tubes in his laboratory, Dr. Roentgen discovered a new form of electromagnetic radiation. This radiation could penetrate solid materials such as limbs, leaving behind an image on photographic plates [3]. This discovery, later named X-rays, formed the foundation for modern radiology and early radiation therapy. Shortly after Roentgen's work, the work of a Nobel prize-winning physicist couple, Marie and Pierre Curie on radiation-producing uranium salts led to the discovery of the radioactive element radium [3]. The high levels of radiation emitted from radium were used in the treatment of various cutaneous cancers, yielding promising results. These two discoveries accelerated the application of radiation in the treatment of numerous medical conditions.

Likely the most important advancement in the field of radiation therapy was the clinical application of linear accelerators (linac). Decades prior to this, high-energy particle accelerators were theorized and eventually developed by physicists. As these devices became more efficient, they were adopted by early pioneers of radiation oncology for their use in cancer treatment. In 1953, the first clinical linac was installed at the Hammersmith Hospital in London, England [4]. The success of clinical linacs is due to their ability to deliver high-energy radiation beams in a more precise manner to maximize tumor damage while limiting damage to healthy tissues. Around the time linear accelerators were making their way into hospitals, scientists and clinicians began to deepen their understanding of the interaction between radiation and living cells. This is known as the study of radiobiology. The decades following these milestone events have produced numerous advancements in the field of radiation oncology.

Fig. (1). Portrait of Wilhelm Roentgen, late 19th century(Commercial license purchased for image through istockphoto.com).

Mechanisms of Radiation Therapy

Effective DNA repair mechanisms are an important safety net in healthy cells to preserve their genome from the estimated 100 thousand spontaneous or induced DNA lesions that occur daily [5]. The study of radiobiology has shown that cancerous cells are more susceptible to lethal DNA damage from radiation compared to their healthy counterparts. This is a result of unique characteristics found in a majority of cancer cells that aid in their ability to proliferate.

Sensitivity to DNA damage changes with the cell cycle phases; G2 and M phases are the most sensitive, while S phase is the most resistant due to active DNA synthesis and increased activity of DNA repair mechanisms (Fig. **2**) [6]. Due to the rapid proliferation of most cancer cells, they can be found in these sensitive phases more often, making them susceptible targets for radiation-induced DNA damage. When DNA damage occurs, cancer cells typically have a reduced ability to repair it compared to healthy cells [7]. This is largely due to mutations in genome segments responsible for DNA repair that cancer cells take advantage of to progress into a more aggressive state. An example of this is the well-studied BRCA1 or BRCA2 genes, which are crucial for repairing double-strand DNA breaks and are commonly found in breast and ovarian cancers, leading to increased genetic instability [8].

CHAPTER 6

Effects of Anesthesia on Cancer

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Abstract: The aim of this chapter is to explore the effects of perioperative anesthetic choices on cancer biology and recurrence. By looking at current research, this chapter compares how different anesthetic agents can affect immune function, inflammatory processes, and tumor progression. This chapter compares the effects of intravenous and volatile anesthetics, as well as the effects of commonly used analgesics. The goal of this chapter is to equip clinicians with basic knowledge on these effects to guide the creation of tailored anesthetic strategies in this relatively large patient population. This chapter also emphasizes the need for further research on these effects due to the relative lack of randomized controlled trials.

Keywords: Opioids, Anesthesia, Blood product transfusion, Cancer progression, Ketamine, Propofol, Volatile anesthetics, Wound healing.

INTRODUCTION

The perioperative period is a crucial period for patients undergoing surgery for cancer treatment. Surgery causes systemic inflammation, immunosuppression, and metabolic changes in the body- all of which create an environment susceptible to tumor growth. In addition to surgical stress, anesthetics and analgesics can also influence immune system response, tumor cell angiogenesis, and proliferation, which can potentially lead to tumor recurrence and metastasis. This chapter reviews current evidence on the immunological and oncologic effects of various anesthetics, including volatile and intravenous agents, regional anesthesia, opioids, and adjunctive medications. By exploring the mechanisms through which these agents affect tumor biology—such as changes in immune cell activity, cytokine production, angiogenesis, and gene expression—anesthesiologist can better tailor their plan to optimize perioperative cancer care.

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Volatile Anesthetics and Cancer Progression

Research on the link between volatile anesthetics and cancer development is still in progress. Recent research, however, has revealed that *via* several biological mechanisms, volatile anesthetics may affect cancer outcomes. Volatile anesthetics can compromise the immune system and encourage tumor growth, therefore increasing the chance of metastases and worsening the long-term cancer prognosis [1].

Proinflammatory Effects and Immunomodulatory Actions

Volatile anesthetics such as isoflurane and sevoflurane impact the immune system by changing the balance between T-helper 1 (Th1) and T-helper 2 (Th2) cells. While Th1 cells more actively contribute to anti-inflammatory actions, Th2 cells help to induce inflammation. Research on volatile anesthetics has revealed a stronger drive toward a Th2-dominant immune response [2]. For instance, research by Ji *et al*. revealed that during surgery, the Th1/Th2 ratio was much reduced by sevoflurane [3]. In a similar context, Saha *et al*. found that isoflurane lowered CD4+ T-helper cell numbers, most likely in response to elevation of anti-inflammatory cytokines, creating a Th2-dominant immunological response that might promote tumor growth and spread [4]. Volatile anesthetics have also been shown to reduce another key lymphocyte of the innate immune system, natural killer (NK) cells. NK cells play a crucial role in tumor surveillance and control of infections. This suppression is partly mediated through the inhibition of adhesion molecules such as leukocyte function-associated antigen-1 (LFA-1). LFA-1 is crucial for natural killer (NK) cell activation and their ability to kill target cells. It facilitates the formation of the immunological synapse and promotes adhesion between NK cells and their targets [5]. Though they do not change the degranulation process, volatile anesthetics reduce NK cell activity by interfering with their capacity to form efficient conjugations and polarizations with target cells [5]. Reduced NK cell activity during the perioperative phase could help to explain higher susceptibility to tumor spread and infections.

Using volatile anesthetics lowers the quantity and activity of circulating natural killer (NK) cells both during and after surgery, therefore perhaps causing immunosuppression [6].

Impact of Cellular Apoptosis and Tumor Proliferation

Volatile anesthetics have been shown to induce apoptosis in major components of the immune system, such as T cells and B cells, *via* a mitochondria-dependent caspase-mediated pathway [7]. The mitochondria-dependent caspase pathway is a critical apoptotic process in which mitochondria cause cell death by releasing

proteins into the cytoplasm, which activates caspases [7]. These effector caspases subsequently execute cell death by cleaving a range of proteins, resulting in DNA breakage and cell shrinkage [7, 8].

Across several cell types and tissues, volatile anesthetics have been demonstrated to potentially upregulate hypoxia-inducible factors (HIFs), particularly HIF-1α. HIFs a transcription factor that enables cells to tolerate low oxygen levels (hypoxia), specifically fast-expanding tumors that exceed their blood supply [9]. In a study by *Qi Fang Li*, Hep3b cells, a human hepatocellular carcinoma (HCC) cell line, were exposed to volatile anesthetics [9]. In their study, when Hep3B cells were exposed to isoflurane, it stimulated a time- and concentration-dependent increase in HIF-1α protein levels [9]. This upregulation of HIF-1α enhances the expression of several downstream target genes, including heme oxygenase 1, inducible nitric oxide synthase, and vascular endothelial growth factor (VEGF) [9]. Furthermore, the elevation of VEGF helps new blood vessels to develop. These new capillaries stimulate additional development and provide routes for tumor cells to enter the bloodstream (metastasis).

Volatile anesthetics have also been shown to enhance the transcription of pro-metastatic factors such as MMP-2 and MMP-9. MMP2 and MMP9 are matrix metalloproteinases, a type of enzyme that is essential for tissue remodeling and breakdown [10]. Both take part in a number of physiological and pathological processes, such as angiogenesis, cancer metastasis, and wound healing. It has been observed that sevoflurane and isoflurane increase MMP-2 and MMP-9 expression [10 - 12]. On the other hand, conflicting results also imply that volatile anesthetics like desflurane and sevoflurane can inhibit tumor cell invasion and lower MMP-9 secretion in specific situations, like colorectal cancer cells [13]. Depending on the cancer type and anesthetic used, these two studies demonstrate the intricate and context-dependent effects of volatile anesthetics on the transcription of pro-metastatic factors, which may either encourage or inhibit tumor progression.

The ability of volatile anesthetics to upregulate the expression of PD-L1 on tumor-associated macrophages supports the immunosuppressive properties of volatile anesthetics. PD-L1 stands for Programmed Death-Ligand 1, a protein that helps regulate immune responses [14]. It is a type of immune checkpoint molecule that helps control how strong the immune system's attack on cancer cells. Essentially, PD-L1 acts as a brake on the immune system [14]. This modification of the tumor microenvironment fosters an immunosuppressive milieu, which may promote the survival of tumor cells and facilitate metastasis in the post-surgical period.

CHAPTER 7

Anesthesia Evaluation of Cancer Patients Prior to Surgery

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Abstract: The population of cancer patients and the procedures they undergo have been increasing over the years. Knowing how cancer affects patients is important for perioperative anesthetic management. This chapter will describe the importance of the preoperative evaluation of cancer patients and their perioperative implications. Besides their primary cancers, these patients often have comorbidities, treatment regimens, and side effects that can affect the anesthetic plan. This chapter will explore the different organ systems affected by cancer and the perioperative considerations for the anesthesia provider.

Keywords: Airway assessment, Chemotherapy, ERAS, Frailty, Fibrosis, Hepatotoxicity, Malnutrition, Nutrition, Nephrotoxicity, Paraneoplastic syndrome, Preoperative evaluation, Radiation.

INTRODUCTION

Cancer is the second leading cause of death in the United States, with an estimated incidence of 1,958,310 cases in 2023 [1]. It has a broad clinical presentation, which includes symptoms associated with its location and spread, paraneoplastic syndromes not directly caused by the tumor, and side effects from cancer treatments such as chemotherapy or radiation.

Preoperative evaluation of the cancer patient is a multistep process that allows the anesthesiologist to both gather important medical history and develop a comprehensive intra- and postoperative management plan. Other objectives include conducting a physical exam, obtaining informed consent, and educating the patient or family on the proposed surgery and perioperative care plan [2]. This chapter examines key aspects of the preoperative evaluation of cancer patients and their impacts on anesthesia management.

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Airway Assessment

Cancer patients may have anatomical and physiological changes that complicate airway management. Tumors in the head, neck, or thoracic region can cause obstruction, restricted mouth opening, tracheal deviation, or airway compression. Earlier radiation therapy can lead to fibrosis, increased bleeding, and reduced tissue elasticity, making intubation challenging. Therefore, preoperative airway assessment is a critical component of anesthesia planning, particularly in cancer patients who may present with unique challenges due to tumor-related airway compromise, prior treatments, or anatomical changes. A thorough evaluation allows anesthesiologists to anticipate difficulties, select appropriate airway management strategies, and reduce perioperative risks [2].

Evaluation should begin with a comprehensive history to assess for comorbidities and signs of airway obstruction, including stridor, dyspnea, orthopnea, dysarthria, dysphagia, or voice changes. This should also include a history of prior surgeries, previous radiation or chemotherapy, and alcohol, tobacco, or substance use. If available, reviewing medical records for prior issues with anesthesia or difficult intubation can help guide management [3].

A thorough physical exam should include Mallampati classification, mandibular protrusion, thyromental distance, neck mobility, and auscultation of the neck for stridor. Doctors also inspect the oral cavity for tissue friability, scarring, anatomical irregularities, lesions, burns, excess mucus, or signs of infection. If airway compromise is suspected, reviewing prior imaging studies (CT/MRI) or a flexible nasopharyngoscopy may be needed to evaluate upper airway tumors.

Access/Line Placement

Vascular access is a crucial aspect of perioperative care in cancer patients, who often require long-term intravenous therapy, chemotherapy, and complex surgical procedures. These patients may present with challenges such as difficult peripheral venous access, prior central line placements, and chemotherapy-induced vascular damage [4]. A thorough preoperative vascular access evaluation allows anesthesiologists to anticipate complications, select the most appropriate access method, and optimize patient safety.

Management should be guided by the patient's overall health status, the type and duration of the planned surgery, and ongoing oncologic therapies. Many cancer patients require major procedures that involve significant fluid and electrolyte shifts, blood loss, or intraoperative chemotherapy. Peripheral IV access is the most common first step and may be adequate for minor procedures. Increasing the number or size of peripheral IVs may provide sufficient access for moderately

invasive surgeries, depending on the type of procedure and the patient's other comorbidities.

For major surgeries such as those involving the thorax, abdomen, or head and neck, more secure access, such as a central venous line or peripherally inserted central catheter (PICC), may be needed. Central lines such as internal jugular, femoral, or subclavian catheters are ideal options for patients with difficult or limited peripheral access and provide stable access for fluid resuscitation, TPN, vasoactive drug administration, and central venous pressure monitoring [4]. For surgeries with significant anticipated blood loss, prolonged operative times, or patients requiring close hemodynamic monitoring, an arterial line may be indicated. This allows frequent blood sampling and arterial blood gas monitoring to guide intraoperative management.

Overall, vascular access is of critical importance to the successful management of oncology patients during the perioperative period. Access selection must be individualized based on patient history, including previous treatments, type and duration of surgery, and comorbidities.

Nutrition/Fasting/Electrolytes

Nutrition plays a critical role in the anesthetic management of cancer patients. Malnutrition and cachexia are common in this population due to treatment side effects, decreased oral intake, and metabolic demands of the disease itself. Because poor nutritional status is associated with increased morbidity and delayed recovery, it is important to identify malnourished patients and optimize nutrition with a structured preoperative diet, counseling, and supplementation in the perioperative period.

Fasting guidelines must be carefully balanced in cancer patients to reduce the risk of aspiration while minimizing the negative metabolic effects of prolonged fasting. The American Society of Anesthesiologists (ASA) standard preoperative fasting recommendations typically allow clear fluids up to 2 hours before anesthesia and a light meal up to 6 hours prior (Table **1**). However, individualized fasting plans may be necessary in cancer patients, especially those with gastrointestinal tumors, decreased motility, or delayed gastric emptying. For patients receiving enteral nutrition *via* feeding tubes, fasting recommendations should be modified based on the type of formula and the patient's current health status.

Enhanced Recovery After Surgery (ERAS) protocols increasingly advocate for preoperative carbohydrate loading and minimal fasting to preserve lean body mass and improve insulin sensitivity [5]. While this approach is generally safe and

CHAPTER 8

Unique Anesthetic Considerations in Cancer Patients

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Abstract: In this chapter, we examine how unique situations arise in cancer patients and how they affect anesthetic management. The conditions include septic and obese patients, cancer-causing paraneoplastic syndromes such as Cushing's and Lambert-Eaton Syndromes or tumor compression causing mesenteric ischemia. Finally, we examine anesthetic options for patients undergoing stem cell transplantation.

Keywords: Cushing's syndrome, Lambert-Eaton myasthenic syndrome, Mesenteric ischemia, Obese patient, Paraneoplastic syndromes, Stem cell treatment, Sepsis, Tumor compression, Unique anesthesia consideration.

INTRODUCTION

The anesthetic management of cancer patients is a complex challenge that requires an understanding of the relationship between malignancy, comorbid conditions, and the body's response to surgical stress and anesthetic agents. Cancer, along with the associated treatments, can significantly alter physiological systems requiring specialized and individualized anesthesia techniques. This chapter explores the unique anesthetic considerations involved in caring for cancer patients, with a focus on systemic and comorbid conditions, tumor compression, paraneoplastic syndromes, and specialized anesthetic management techniques.

Systemic and comorbid conditions, such as sepsis and obesity, are common among cancer patients and pose significant challenges to anesthesiologists. Sepsis, a critical and often life-threatening condition, can cause profound physiological

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instability, while obesity introduces additional concerns, including respiratory compromise and cardiovascular strain. These conditions require meticulous perioperative management to optimize patient outcomes.

Another crucial aspect of anesthetic management in cancer patients involves the effects of tumor compression, such as in the case of a mediastinal mass. Tumor-induced anatomical changes can directly affect airway, cardiovascular, and neural function, and require careful planning to mitigate risks during surgery and anesthesia.

Additionally, paraneoplastic syndromes can further complicate anesthetic management. These syndromes, often overlooked or misdiagnosed, can manifest with neurological and endocrine disruptions that must be carefully considered when choosing anesthetic agents and monitoring parameters.

Lastly, specialized anesthetic management techniques are required in certain surgical situations. Each of these conditions presents its own unique set of challenges, ranging from optimizing fluid resuscitation and hemodynamic stability to managing organ function and preventing complications.

In this chapter, we will explore these critical topics, emphasizing the need for a comprehensive, patient-tailored approach to anesthetic care. By understanding the multifactorial nature of cancer and its associated conditions, anesthesiologists can enhance the safety, comfort, and outcomes of cancer patients undergoing surgical interventions.

SYSTEMIC AND COMORBID CONSIDERATIONS IN CANCER PATIENTS

Cancer patients often present with a unique set of challenges when it comes to anesthetic management due to the presence of systemic conditions and comorbidities that can significantly impact perioperative care. Among these, sepsis and obesity are particularly critical factors that require careful consideration in the perioperative period. Both conditions can compromise the body's response to anesthesia, complicate surgical outcomes, and increase the risks of intraoperative instability and postoperative complications.

Sepsis

Sepsis is a leading cause of mortality, with a thirty-day mortality rate of 24.4% for sepsis and 34.7% for septic shock, it is an emergency that calls for early detection and rapid treatment [1]. While sepsis mortality rates are high in all cases, patients with cancer are more likely to develop sepsis, and the mortality from sepsis in

such patients is significantly higher [2]. Treatment for sepsis can vary, as no pharmacologic intervention has been shown to consistently reduce mortality [2].

The first six hours of resuscitation of patients with sepsis are referred to as the golden hours due to the critical nature of the disease, to provide the patient with the highest chance of survival. Pre-operative treatment of patients with sepsis includes assessment and optimization. Prior to induction, anesthesiologists must ensure that the patient is as stable as possible to reduce the risk of complications during surgery. This includes ensuring hemodynamic stability, respiratory stability, renal function, and infection control. IV antimicrobial therapy should be administered immediately after the diagnosis of sepsis or septic shock is made. Currently, there is no benefit for delaying treatment until culture results or the start of surgery [3, 4].

Hemodynamic optimization in a timely manner is critical as treatment before organ failure can reduce mortality by 23% compared to patients treated after the onset of organ failure [1]. Hypovolemia can be corrected with a balanced crystalloid solution of up to 30 ml/kg during the first three hours. A patient is determined to be responsive if there is an increase in stroke volume of more than 10-15%. Alternative measures of determining responsiveness can be an increase in pulse pressure of >10% [1].

Respiratory function must also be monitored to avoid respiratory depression and injury during ventilation. Patients with sepsis may have comorbid conditions such as acute respiratory distress syndrome (ARDS), lung inflammation, or metabolic acidosis, which can alter the patient's respiratory function compared to baseline [1]. Therefore, physical examination as well as chest imaging are critical to identifying and treating lung injury.

For elective patients, de-nitrogenation of the lungs with patients breathing 100% O2 through a tightly fitted facemask for up to 3 minutes is recommended. However, patients with sepsis or septic shock often require emergent surgical intervention, making modified rapid sequence induction the preferred approach for initiating general anesthesia. Depending on the urgency and their laboratory values, succinylcholine or rocuronium can be used to facilitate tracheal intubation. Given the frequent presence of hemodynamic instability and compromised hepatic and renal function in septic patients, it is crucial to account for these alterations during induction, as both intravenous and inhalational agents can exacerbate myocardial depression or vasodilation [4]. Induction of anesthesia can be done with commonly used agents such as propofol or with more cardiovascular stable agents such as etomidate or ketamine. Current evidence does not clearly favor one over the other, but care should be taken to use smaller doses given the

CHAPTER 9

Post Operative Care of Cancer Patients

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Abstract: Postoperative management of cancer patients demands a nuanced and collaborative approach, extending beyond the operating room to ensure optimal outcomes. Anesthesiologists play a pivotal role in managing pain, minimizing complications, and supporting early recovery and rehabilitation. This chapter explores evidence-based strategies, including Enhanced Recovery After Surgery (ERAS), multimodal analgesia, and regional anesthesia techniques. It also highlights the importance of psychological support, nutritional optimization, complication prevention, and long-term pain and palliative care. The chapter highlights the anesthesiologist's unique position to lead multidisciplinary teams in delivering comprehensive, patient-centered postoperative care for oncology patients.

Keywords: Cancer recovery, ERAS, Multimodal analgesia, Opioid-sparing strategies, Pain Management, Postoperative care, Palliative care, Regional anesthesia.

INTRODUCTION

The anesthesiologist’s role in the care of surgical cancer patients does not end when the patient leaves the operating room. Postoperative management represents a critical extension of perioperative care—particularly for oncology patients, whose complex needs demand vigilance, precision, and a personalized approach. These patients often arrive at the operating table with a host of pre-existing challenges stemming from chemotherapy, radiation, immunosuppression, and chronic cancer pain [1]. Each of these factors increases the risk of complications and demands that require coordinated postoperative care.

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POSTOPERATIVE PAIN MANAGEMENT: A CENTRAL CONCERN

Managing Pain in Cancer Patients

Postoperative pain in cancer patients is layered atop other types of pain, such as tumor-related pain, chemotherapy-induced neuropathy, post-radiation fibrosis, or chronic pain syndromes from prior cancer surgeries [2]. This pain can be intensified by both the surgery and pre-existing opioid tolerance in patients who have relied on chronic opioid therapy. These patients may benefit from a multimodal approach, which may include techniques such as regional anesthesia and the use of ketamine as an adjuvant to pain control.

Early Recovery after Surgery

Enhanced Recovery After Surgery (ERAS) is an evidence-based multidisciplinary approach to perioperative care that aims to reduce surgical stress, maintain physiologic function, and accelerate recovery [3]. In cancer patients, ERAS has added value as it addresses the increased risk of complications, chronic pain, and prolonged hospitalization. This protocol integrates multimodal analgesia, early ambulation, nutritional optimization, and psychological support.

Multimodal opioid-sparing pain management strategies are particularly emphasized in ERAS and critical in cancer patients who are already immunocompromised or at higher risk for postoperative complications [4, 5]. Non-opioid adjuncts such as acetaminophen, NSAIDs, gabapentinoids, NMDA antagonists like ketamine, and alpha-2 agonists such as dexmedetomidine are commonly used [6].

Regional techniques such as thoracic epidurals, paravertebral blocks, TAP blocks, or PECS blocks are frequently included in ERAS pathways for cancer surgeries [7]. These approaches reduce opioid consumption, enhance mobilization, andimprove postoperative outcomes.

Preoperative optimization, including nutrition and physical conditioning, is crucial, and psychosocial counseling can prepare the patient for both the physical and emotional stress of surgery [8].

Multimodal Analgesia

Multimodal analgesia is the cornerstone of postoperative pain management in cancer patients. This approach leverages the synergistic effects of combining various analgesic agents to reduce opioid requirements and improve pain control [5]. Drugs such as acetaminophen, NSAIDs, gabapentinoids, ketamine, and

dexmedetomidine can be combined in carefully titrated regimens [6]. Regional anesthesia also plays a pivotal role—catheters placed for continuous peripheral nerve blocks or epidural infusions can provide sustained relief during the acute postoperative period [7].

Tailoring Opioid Use

In opioid-tolerant patients, anesthesiologists must anticipate higher analgesic needs. They may incorporate patient-controlled analgesia (PCA), long-acting opioids, and adjuncts such as ketamine and dexmedetomidine infusions to enhance analgesia and reduce side effects [4]. Coordination with the chronic pain or palliative care team is essential.

Neuropathic Pain Management

Neuropathic pain, a common feature in oncology patients, often responds poorly to opioids and instead requires agents like gabapentinoids, serotonin-norepinephrine reuptake inhibitors (SNRIs), or tricyclic antidepressants [2]. Care must be taken to balance efficacy with side effect profiles. In severe cases, interventional techniques such as epidural steroid injections, nerve blocks, or intrathecal therapies may be considered [9].

POSTOPERATIVE COMPLICATIONS IN CANCER PATIENTS

Nausea and Vomiting (N/V)

Cancer patients are predisposed to postoperative nausea and vomiting (PONV), particularly if they have had previous chemotherapy. Preventive strategies include multimodal antiemetics, minimizing opioid use, and using total intravenous anesthesia (TIVA) when appropriate [10].

Infection Control

Anesthesiologists must remain vigilant for signs of infection, given the immunosuppressed state of many patients with oncology. Strict aseptic technique, perioperative antibiotics, and glycemic control are critical [1].

Wound Healing Delays

Poor wound healing is common in patients undergoing chemotherapy or radiation therapy. Nutritional optimization, adequate pain control to allow movement, and attention to pressure points are key factors in prevention and management [1].

CHAPTER 10

The Pediatric Cancer Patient

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Abstract: Children with cancer have a number of pre- and perioperative risk modifiers when they undergo surgical procedures. These can be a direct result of their pathology or treatment and can persist for years after the completion of therapy. In this chapter, we explore the various sequelae of the most common pediatric malignancies and the anesthetic considerations required to deliver optimum care to this vulnerable population.

Keywords: Pediatric anesthesia, Anesthesiology, Oncology, Cancer, Chemotherapy, Hematology, Leukemia, Lymphoma, Neuroblastoma, Radiation therapy, Wilms tumor.

INTRODUCTION

Pediatric oncology patients are a subset of cancer patients who require knowledge of both children and their unique disease pathology to administer anesthesia safely. While these patients are rare, with approximately 1 in 285 children being diagnosed before the age of 20 [1], and the 5-year survival is over 80% in developed countries [2], cancer is still the second leading cause of pediatric mortality, second to trauma [3]. Childhood cancer carries a range of pathologies, and the peak incidence of various malignancies varies by age. The most common oncologic pathologies for all pediatric patients are hematologic, central nervous system tumors, and lymphoma [4, 5]. These children undergo a variety of procedures during workup, treatment, and post-therapy that require anesthesia. In the following chapter, we will explore the various sequelae that the anesthesiologist must consider in the most prevalent pediatric malignancies to deliver safe, optimal care in this vulnerable population.

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ORGAN SYSTEM CONSIDERATIONS

Neurologic

Primary intracranial tumors are the most common pediatric solid cancers, with astrocytomas accounting for over half of these neurologic malignancies [6, 7]. These patients typically present with signs and symptoms of increased intracranial pressure (ICP), including vomiting, irritability, altered mentation, and macrocephaly [8, 9]. Older children may report nausea, headache, and vision changes [8, 9]. Focal neurologic findings such as seizures, gait disturbances, and hemiparesis may also be present, indicating significant mass effect [10, 11]. Spinal tumors are uncommon, but those patients may have signs of spinal cord compression, including gait changes, extremity weakness, and, in older children, new onset incontinence [12].

Neurologic toxicity from chemotherapy is common, and symptoms can be a multifactorial result of both malignancy and constitutional dysfunction from treatments [11]. Platinum agents, L-asparaginase, methotrexate, cyclosporin, and a host of other chemotherapeutic drugs are the most likely to cause direct central toxicity and are typically dose-limited and reversible [13]. Leukoencephalopathy, vision loss, ototoxicity, and peripheral neuropathy from cisplatin and vincristine are all possible chronic chemotherapy-induced neurotoxicities unrelated to the patient's underlying disease process [14]. Radiation therapy has been documented to cause focal necrosis, myelitis, stroke, seizures, and chronic vision changes even at relatively small doses [13, 15].

Anesthetic Considerations

Total tumor resection is the principal treatment for neurologic malignancies [16]. Increased ICP can be an immediate danger to these children. The risk of premedication and sedation must be weighed with the risk of preinduction intravenous access and patient irritation, as both plans can result in worsening ICP [17]. Careful titration of premedication allowing for quick induction, intravenous access, and intubation is required to control end-tidal carbon dioxide (CO2) and cerebral blood flow (CBF). As such, all patients with concerns for increased ICP require a definitive airway, avoiding profound hypertension during laryngoscopy, which again would further increase CBF and ICP.

Cardiac

Cardiac sequelae from malignancy in children are usually the result of noncardiac cancers, as primary cardiac tumors are uncommon [18]. When rhabdomyomas, fibromas, teratomas, or myxomas do occur, they have a high survival rate and

may regress spontaneously or with medical treatment [19]. Noncardiac cancers cause cardiac dysfunction *via* several pathologies, including anterior mediastinal masses, pericardial effusions, or hypertension, and side effects of cancer therapies can cause cardiomyopathy and heart failure [20 - 22]. Cancer survivors have a 30-year increased risk of chronic cardiac disease, including coronary artery disease, cerebral vascular disease, and heart failure [22]. The anthracyclines, specifically the cytostatic antibiotics such as doxorubicin, are the most cardiotoxic, suspected to be related to free radical generation, interfering with myocyte metabolism [15, 23]. Mitoxantrone cardiac toxicity has been compared to anthracyclines [24].

Anterior Mediastinal Mass

Perhaps the most feared tumor for the anesthesiologist is the anterior mediastinal mass. Primary or metastatic disease of the chest organs, lymph nodes, or thymus can cause compression of the great vessels, tracheobronchial tree, or heart chambers, leading to dangerous hemodynamic compromise [9, 25]. Lymphomas are the most common malignancies causing anterior mediastinal masses, which are present at the time of diagnosis [26]. Patients can present with a spectrum of symptoms, including dyspnea, orthopnea, stridor, wheezing, or superior vena cava syndrome [11].

Pericardial Effusion

Pericardial effusions occur as a result of infection, obstruction, pericardial metastasis, or cancer treatment (Diamond 2018). Hematopoietic stem cell treatment and mediastinal tumors are the most common causes of pericardial effusions [27]. The presentation may be similar to an anterior mediastinal mass or intracardiac tumor and will vary depending on the degree of tamponade physiology.

Anesthetic Considerations

Anterior mediastinal masses may require tissue biopsy for definitive diagnosis before treatment can begin to try to shrink the tumor burden [28]. A CT scan is recommended for all patients with a suspected anterior mediastinal mass to assess anatomic location and involvement with surrounding structures [28]. A CT scan may also reveal pericardial or pleural effusions that may further hone the anesthetic plan, although the clinical symptoms may not match the radiographic findings [29, 30]. Transthoracic echocardiography may give important information regarding great vessel or heart compression and mass effect on ventricular function and should be considered in all patients with cardiovascular symptoms or those unable to give an accurate history [25, 30]. It is important to

CHAPTER 11

Cancer Patients and Critical Care

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Abstract: Advances in both detection and management strategies have improved survival rates among cancer patients. As a result, more patients may benefit from ICU admission over the course of their disease. Considerations for admission to ICU should include both the short- and long-term prognoses as well as the reversibility of the acute illness. Cancer patients may be admitted to the ICU for a host of reasons, which may be due to the underlying malignancy, treatment related effects, or non-oncologic acute illnesses. Regardless of the indication for admission, these patients require complex coordination of care and a thoughtful and methodical approach to their ICU management.

Keywords: Acute respiratory failure, Cardiac tamponade, Cytokine release syndrome, Hypercalcemia, Hyperleukocytosis, Immune effect cell-associated neurotoxicity syndrome, Leukostasis, Neutropenic fever, Superior vena cava syndrome, Tumor lysis syndrome.

INTRODUCTION

Historically, the admission of cancer patients to the intensive care unit (ICU) has been widely debated. Reasons cited include the depletion of already limited resources and anticipated poor outcomes [1, 2]. However, advances in cancer therapies and early detection methods have improved overall survival rates [3, 4]. Not only that but studies have shown that the survival rate of cancer patients requiring ICU admission has also increased. Proposed reasons include advances in both oncologic therapies and management of organ dysfunction [5]. As a result, the number of cancer patients who may benefit from ICU admission has substantially increased [1, 4].

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TRIAGE AND PROGNOSTICATION

Triage of the critically ill cancer patient is quite complex. Predicting which patients will benefit from ICU admission can be challenging. The decision of whether a cancer patient should be admitted to the ICU should take into account the short-term intensive care prognosis as well as the patient's long-term prognosis and anticipated quality of life [6]. In general, ICU admission should be considered if the patient has a reversible condition and his or her oncologic prognosis justifies aggressive therapies [6]. Of course, this is assuming that ICU admission is within the patient's goals of care.

Prognostic scores are often used to predict outcomes and aid in clinical decision making within the general ICU population. However, studies assessing the utility of these scores in cancer patients are limited and the results have been mixed [7 - 10]. Soares *et al* conducted a prospective study assessing the performance of 5 general severity of illness scores (Acute Physiology and Chronic Health Evaluation II and IIIJ (APACHE II/IIIJ), Simplified Acute Physiology Score II (SAPS II), Mortality Probability Models at admission and 24 hours (MPM0/24)) and one cancer-specific predictive model (ICU Cancer Mortality Model (ICMM)). They found that none of the scoring models accurately predicted mortality in the critically ill cancer patients [7]. Similarly, Schellongowski *et al* found that while the APACHE II, SAPS II, and ICCM scores could accurately describe the severity of illness and predict outcomes within a group of cancer patients, they failed to reliably predict individual prognosis [8]. Interestingly, both groups also found that the ICCM, which is a cancer-specific predictive model that takes into account hospital days prior to ICU admission, did not perform better than general predictive models [7, 8].

Studies looking at predictors of short-term prognosis among cancer patients admitted to the ICU have identified several risk factors associated with increased mortality. These include severity and number of organ failures, acute respiratory failure, need for mechanical ventilation, late ICU admission, the need for vasopressor support, and performance status prior to admission [6, 11, 12]. The development of acute respiratory failure has been identified as the most important risk factor for mortality in critically ill cancer patients [6, 13]. In contrast, the stage of malignancy has little to no effect on short-term survival [12, 14]. However, the primary determinants of long-term outcomes in this patient population relate to the characteristics of the underlying malignancy [6, 14].

Studies have demonstrated the inadequacy of ICU admission triage criteria, particularly in cancer patients' population. In a prospective study by Thiery *et al*., 20% of patients denied ICU admission because they were deemed "too well" and

died before discharge. Similarly, 25% of the patients, not admitted to the ICU because they were "too sick", survived [5, 15]. As a result, some have called for broader ICU admission criteria among the cancer patient population. In response to this, an international expert consensus released evidence-based ICU admission criteria recommendations for critically ill cancer patients. While these recommendations are evidence-based, they are founded mostly on observational studies. The recommendations place patients into one of three categories: full code management, ICU trial, or no ICU admission. Patients recommended for full code management include patients with a newly diagnosed cancer with expected survival of longer than 1 year, patients whose cancer is in remission, and patients with malignancies that have either curative therapies or therapies, which can extend survival beyond one year [5, 6]. The guidelines recommend not pursuing ICU admission whenexpected survival is less than one year despite ongoing treatments, when there are no further life-extending treatments available, and when the patient has a poor functional status [6]. Outside of these specific circumstances, an ICU trial is suggested. An ICU trial consists of initial unlimited ICU support followed by re-evaluation after a period of 3-5 days. The recommendation of 3-5 days is based on data that suggests that only after 3 days could the degree of organ dysfunction differentiate between survivors and non-survivors [5, 6, 16].

INDICATIONS FOR ICU ADMISSION

Cancer patients comprise 15% of all ICU admissions [17, 18]). Solid organ malignancies are more commonly encountered than hematologic malignancies. Lung cancer is the most common solid organ malignancy seen in cancer patients admitted to the ICU while leukemia and lymphoma are the most common hematologic malignancies identified [12, 19]. Reasons for admission to the ICU can be divided into malignancy related, cancer therapy related, and acute illness unrelated to malignancy [12]. The most common indications for ICU admission in cancer patients are post-operative recovery, respiratory failure, and sepsis [4, 20]. In a prospective study by Soares *et al* looking at characteristics of cancer patients requiring ICU admission, post-operative care represented 57%, acute respiratory failure represented 10%, and sepsis represented 15% of ICU admissions [20].

Malignancy Related Indications

Acute cancer-related complications often necessitate ICU admission in both solid organ and hematologic cancer patients. Some complications are common to all types of malignancy whereas others may be attributed to a specific subtype.

CHAPTER 12

Anesthetic Management of Major Cancer Related Surgical Procedures, Part 1: Thoracic and Neurological Procedures

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Abstract: In this chapter, we will look at the anesthetic considerations and techniques that facilitate the safe and successful operative care of thoracic and neurologic tumors. Modality and drug choice will be discussed in both the context of hemodynamic stability and tumor effects. Additionally, airway management, vascular access, and invasive monitoring may change based on tumor type and location, along with patient presentation. The goal of this chapter is to provide the non-fellowship-trained anesthesiologist with a basic understanding of how to safely care for patients undergoing care that they may not commonly provide.

Keywords: Activated clotting time, Bronchial blocker, Double lumen endotracheal tube, One lung ventilation, Pulse pressure variation, Retrograde autologous priming, Sarcoma, Transesophageal echocardiography.

INTRODUCTION

Providing care for patients with thoracic tumors is a complex and challenging aspect of anesthesia practice. The tumors can broadly be categorized by anatomical location as follows:

1. Lung Tumors
2. Mediastinal Tumors
3. Pleural Tumors
4. Chest Wall Tumors
5. Tracheobronchial Tumors
6. Esophageal Tumors
7. Cardiac Tumors

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Anesthetic approaches and specialized techniques depend on the variety and location of the tumor, along with its impacts on respiratory and cardiovascular function, to ensure patient safety and optimize surgical outcomes. This section will provide an overview of the principles, practices, and considerations involved in the anesthetic management of patients undergoing surgical treatment of thoracic tumors.

PREOPERATIVE ASSESSMENT

Medical History

Having a firm understanding of the patient's medical history is essential for formulating an effective and safe anesthetic plan. Patients with thoracic tumors often have significant comorbidities such as chronic obstructive pulmonary disease (COPD), cardiovascular diseases, a history of smoking, significant alcohol use, antiplatelet therapy, *etc*. All of which can significantly affect anesthetic management.

Physical Examination

A comprehensive physical examination should focus on the respiratory and cardiovascular systems. Evaluation of airway patency, lung function tests, and assessment of exercise tolerance are essential components. Additionally, uncontrolled hypertension (specifically a diastolic blood pressure of 110 mmHg or higher) on the day of surgery may merit postponing the procedure as this can lead to poor outcomes, including but not limited to uncontrollable intra- or postoperative bleeding, increased thirty-day mortality, cerebrovascular accidents (CVA), and myocardial infarction (MI).

Diagnostic Tests

Preoperative diagnostic tests such as chest X-rays, CT scans, MRI, and PET scans provide information on tumor location, size, and potential metastasis. Pulmonary function tests, arterial blood gases, and echocardiograms offer insights into the patient's baseline respiratory and cardiac status. However, basic blood work such as complete blood counts (CBC) and comprehensive metabolic panels may be even more valuable for intraoperative anesthetic management as they may reveal electrolyte and metabolic disturbances related to various cancer syndromes. These disturbances can lead to hemodynamic instability that is refractory to treatment other than correcting the disturbance itself.

ANESTHETIC PLAN

Choice of Anesthetic Technique

The choice between general anesthesia, regional anesthesia, or a combination of both depends on the tumor's location, the surgical procedure, and the patient's overall health status. General anesthesia is typically required for thoracic surgeries, while regional techniques, such as epidural or paravertebral blocks can provide effective analgesia. Although regional techniques may be contraindicated if the patient is unable to hold antiplatelet therapy or if heparinization is necessary for the procedure.

Airway Management

Airway management poses significant challenges in thoracic surgery due to potential airway obstruction by the tumor. Techniques such as double-lumen endotracheal tubes (DL ETT) or bronchial blockers are often employed to achieve lung isolation, which is crucial for surgical exposure and patient safety. However, standard endotracheal intubation is utilized when lung isolation is not required. Placement of a DL ETT starts with selecting an appropriate size based on the height and gender of the patient [1]. The choice of a right or left DL ETT must also be made, but the vast majority of cases can be managed with a left-sided DL ETT if there is no surgical involvement of the left main bronchus.

Patient Factors	DLT Size Recommendations
Height 54-65” 65-70” 71-76”	 35-37 Fr 37-39 Fr 39-41 Fr
Age 8-10 yo 10-12 yo 12-13 yo 13-14 yo	 ~26 Fr ~28 Fr ~32 Fr ~35 Fr

n.b. 26 an 28 Fr DLT are only generally available as left-sided.

To place the DL ETT, direct laryngoscopy is best, and once the vocal cords are visualized, the DL ETT is initially advanced with the curvature to the patient's right side. As the tip passes the cords, the DL ETT is rotated 90 degrees counterclockwise as it is advanced, and the stylet is removed. It is also important to ensure the stylet is placed in the bronchial side, as it is generally longer than the tracheal side and can cause perforation. Once the DL ETT is in place, the tracheal

CHAPTER 13

Anesthetic Management of Major Cancer Surgical Procedures Part 2: Breast, Female Reproductive Organs, Prostate, Testicular, and Renal Cancers

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Abstract: This chapter discusses the anesthetic management of major cancer surgeries involving the breast, female reproductive organs, prostate, testicle, and kidney. The focus will begin in the pre-operative area, addressing concerns for these patients prior to surgery. It will then explore the intraoperative anesthetic management of female and male cancers and their related surgeries. Finally, the chapter will examine the postoperative management of these patients.

Keywords: Breast cancer, Cervical cancer, Female reproductive organs, Intravenous access, Lumpectomy, Lymph node dissection, Mastectomy, Ovarian cancer, Prostate cancer, Trendelenburg.

INTRODUCTION

Surgical procedures can be performed in different settings - an office, an ambulatory surgery center, or a hospital operating room. The decision of where to perform a procedure involves quite a few variables, including the health status of the patient, the type of procedure or surgery, and what equipment is necessary.

The patient's health status is a very important factor in determining whether the procedure can be performed outside the operating room. For anesthesiologists, we evaluate the co-morbid conditions of the patient and classify the patient into the appropriate ASA classification. Usually, an ASA I or II can be safely cared for at an office or surgery center, if the appropriate equipment is available. ASA III patients can often be done at these locations; however, more vigilance needs to be taken to ensure the patient is appropriate for the site.

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For most of the cancers discussed in this chapter, the first step typically involves a tissue sample for diagnosis. Most patients with ASA I or II can safely undergo tissue sampling in an ambulatory setting under mild to moderate sedation. Sometimes, they can even be done under local anesthesia only. General anesthesia is reserved for more complicated cases and would be used at discretion of both the anesthesiologist and surgeon performing the procedure. Patients who have an ASA status of III can also be treated at an ambulatory center but may require a higher level of vigilance, and expectations may need to be set pre-operatively that they may receive less anesthesia due to their medical history. If this is something the patient cannot tolerate, the case can be scheduled at a hospital with appropriate support.

Sometimes, the first professionals in the patient's cancer journey are the staff members who care for them during their initial procedure. Patients who come in for a procedure are often a little uneasy, but patients who come in for any type of procedure that may involve a cancer diagnosis are understandably anxious. Not only do they have fears involving the surgery or procedure itself, but also a real fear of what the diagnosis holds, so care should be taken to make each patient feel safe and comfortable. Patients may also benefit from anxiolytic medications.

Related to anxiolysis, the quickest way to deliver medication is through intravenous access. However, some of these patients, particularly as their cancer treatments progress, may have challenging venous access from genetic reasons or iatrogenic causes, such as chemotherapeutic side effects. Most of the time, the preoperative nursing staff can obtain intravenous access; however, sometimes they are unable to have intravenous access after multiple attempts. At that point, anesthesiologists may be asked to assist in this task and may need to perform ultrasound-guided intravenous insertion. Some patients who are very difficult or are undergoing chemotherapy may come in with a central access line, such as a port, that may be accessed in very difficult circumstances. Once intravenous access is achieved, an anxiolytic agent can be dosed if appropriate. Typically, in the perioperative setting, midazolam is used as the initial medication of choice to provide anxiolysis and amnesia.

Another consideration preoperatively is pre-emptive analgesia. This can be in the form of oral medications, possibly combined with a peripheral nerve block if indicated. There are not many nerve blocks that can be used, but some help mitigate post-operative pain and will be mentioned later in conjunction with the respective cancer discussions. Some of the nerve blocks that will be addressed are pectoralis blocks and transverse abdominus plane blocks, as well as local anesthetic injections by the surgeon. For cases with longer recovery times, some

surgeons may place a pain pump that intermittently gives doses of local anesthetic for several days postoperatively.

Postoperative nausea and vomiting are of significant concern to patients and staff due to the discomfort and possible increased length of stay [1]. This can also be addressed preoperatively with topical patches like scopolamine and newer oral medications like Emend, which can help prevent nausea [1, 2].

Overall, there are several preoperative concerns for the anesthesiologist. From determining where the surgery is to occur, to developing an anesthetic plan that addresses safety, venous access, anxiety, analgesia, and postoperative nausea, there is an array of topics that both the anesthesiologist and patient will encounter related to cancer care.

SURGERIES FOR FEMALE CANCERS: BREAST AND FEMALE REPRODUCTIVE SYSTEMS

Breast surgery is a common surgical procedure for many indications, including biopsy of the breast, benign lump excision, breast cyst/abscess, and cosmetic procedures, but the most common reason is for breast cancer. The prevalence of breast cancer has been increasing, and continues to increase, in the United States, and is known to be one of the leading causes of death in females [3]. Breast cancer can be further classified into different histological and molecular subtypes that determine treatment and prognosis [4].

Types of Breast Surgery

Breast cancer surgery has made many advancements over the past several decades. Originally, total mastectomies were widely performed, but are now not as frequently done, thanks in part to landmark trials that have proven the efficacy of breast conserving treatment or BCT. Examples of BCT include wide local excision of the tumor, in addition to chemotherapy or radiation therapy, in comparison to full mastectomy alone. Wide local excision surgery requires histological confirmation that a minimum margin of typically 5mm of normal tissue has been excised around the tumor. There are contraindications to BCT, however, and these include inflammatory breast cancer, prior radiation to the breast, and multifocal disease [5]. Radical mastectomies are reserved for any tumor that invades the pectoral muscle. Some patients also choose to have a full mastectomy due to personal choice or not being a candidate for BCT. The patients who decide to have prophylactic mastectomies do so for risk reduction and can be simple, skin-sparing, or nipple-sparing mastectomies [6].

CHAPTER 14

Anesthetic Management of Major Cancer Surgical Procedures Part 3: Musculoskeletal, Head and Neck, Hematological, and Endocrine Malignancies

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Abstract: Major oncologic surgeries present unique challenges for anesthesiologists, requiring a deep understanding of the pathophysiology of malignancy, the physiological impact of extensive surgical procedures, and the complexities of perioperative care. The anesthetic management involves a multidisciplinary approach between the surgical team and anesthesia providers. Methodical planning and advanced techniques can lead to optimal management of patients.

Keywords: Adrenalectomies, Airway fire, Amputation, Bone marrow biopsies, Laryngectomy, Limb sparing surgery, Parathyroidectomies, Thyroidectomies, Tracheostomy.

INTRODUCTION

Oncologic surgeries present unique challenges for anesthesiologists, requiring careful consideration of both the underlying malignancy and the physiological demands of complex surgical procedures. This chapter explores the specific nuances associated with musculoskeletal, head and neck, hematological, and endocrine malignancies, focusing on the anesthetic considerations relevant to surgical interventions in each system. Each of these cancer types poses distinct perioperative concerns that must be thoughtfully integrated into the anesthetic plan. The following sections will highlight these challenges and provide guidance for their effective management.

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MUSCULOSKELETAL CANCERS AND ANESTHETIC CONSIDERATIONS

Musculoskeletal cancers involve the bones and soft tissues of the body, which create the musculoskeletal system. These cancers typically produce pain and limit functionality. As surgical management and surgical techniques have been refined, perioperative management has evolved to meet patient needs. In this section, we will discuss the anesthetic management of patients undergoing surgery for musculoskeletal cancers, more specifically, primary bone sarcoma including osteosarcoma, chondosarcoma, and ewing sarcoma, and soft tissue sarcoma.

Primary Bone Sarcoma

Osteosarcoma is the most common primary bone sarcoma [1]. Most patients are diagnosed between the ages of 10 and 19; however, there has been an increase in the diagnosis of patients over the age of 40 associated with Paget's disease. Together with Ewing's sarcoma, these two cancers account for most primary bone cancers in patients under the age of 20. The incidence was the highest in long bones, but the face, skull, and other parts of the skeleton can also be involved [1]. Ewing Sarcoma is an aggressive tumor mostly diagnosed in adolescence. It presents with pain at a local site and typically involves the pelvis, axial skeleton, and femur [2]. Although most diagnoses occur with local infiltration, subclinical metastasis is often present, increasing the chances for relapse.

Chondrosarcoma accounts for the majority of primary bone sarcomas in patients over the age of 40. Unlike osteosarcoma and Ewing's sarcoma, chondrosarcoma involves cartilage, much like the name insinuates. Chondrosarcoma typically involves the central axial skeleton, including the sternum, pelvis, and ribs, but can often be found within the proximal humerus and femur [3].

Limb-Sparing Surgery

The primary surgical intervention for patients with primary bone sarcoma is limb-sparing surgery. The goal is to allow for local resection of the primary tumor and maintain full functionality. The anesthetic plan for these patients can be very complex and does involve discussions with the patient and surgeon for optimal management. A primary focus for these patients is adequate pain management and volume resuscitation. Pre-operative consultation and introduction of regional and neuraxial anesthesia prior to the day of surgery can ease the patient's anxiety. Effective pain management is crucial for early rehabilitation and overall functional recovery [4, 5].

Limb-sparing surgery is determined by anatomical findings on initial imaging. Reconstruction is often avoided, but must be considered based on tumor growth and invasion. The popular reconstruction methods include endoprosthesis, allograft-prosthetic, and biological reconstructions [4]. The final decision lies in the hands of the surgeon, but many factors, including financial cost, durability, infection risk, and evaluation of limb length disparities, help decide the final reconstruction graft type [4].

The type of anesthetic used for limb-sparing surgery depends on the location of the tumor, size of the resection, concern for local vascular involvement and hemodynamic instability, and optimization for post-operative pain. General anesthesia is often considered for complex procedures and those with large fluid shifts. With prolonged procedures, general anesthesia appears to be the safest route to maintain ventilatory support. Neuraxial anesthesia can be considered for shorter procedures, especially for lower extremity surgeries. Due to the large sympathetic blockage that occurs with spinal anesthesia, it may be avoided for concerns of hemodynamic instability. Epidural anesthesia will likely not be sufficient for surgical purposes, but it is optimal for intra-operative and post-operative pain control. Of note, epidural analgesia has the potential effect of causing motor weakness, which may complicate post-operative rehabilitation. Many institutions also prevent patients from getting out of the hospital bed with epidurals in place, further complicating early rehabilitation efforts [4, 5].

In place of epidural analgesia for pain control, regional anesthesia is an effective method to reduce intraoperative pain and enhance postoperative recovery. Various nerve blocks can be utilized for upper and lower extremities [6, 7]. Brachial plexus nerve blocks are utilized for upper extremity procedures, whereas femoral nerve, adductor canal, sciatic nerve (sub-gluteal and popliteal approaches), lateral cutaneous femoral nerve, fascia iliaca, and quadratus lumborum nerve blocks are among the most common lower extremity nerve blocks [6, 7]. Single-shot nerve blocks with ropivacaine or bupivacaine have been effective for pain control but only have significant effects for up to 16 hours. Adjuncts such as dexamethasone, dexmedetomidine, clonidine, phenylephrine, and epinephrine have been used to extend the duration of action to about 24 hours [8]. To achieve longer pain control, nerve catheters have been used for continuous administration of low-concentration ropivacaine. Other options include the use of Exparel, a liposomal bupivacaine, which has been reported to increase the duration to up to 72 hours but does not require a catheter for continuous infusion [9]. There are contradictory studies on the use and efficacy of Exparel with no clear guidelines. Other pain modalities include patient-controlled analgesia, allowing patients to trigger a bolus of opioids intravenously.

CHAPTER 15

Anesthetic Management for Major Surgical Procedures Part 4 – Gastrointestinal Oncology

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Abstract: Gastrointestinal (GI) oncology presents a uniquely complex and evolving landscape for anesthesiologists, requiring a thorough understanding of tumor biology, surgical approaches, and perioperative physiology. This chapter provides a comprehensive overview of anesthetic management in patients undergoing surgery for GI malignancies, including esophageal, gastric, colorectal, hepatobiliary, pancreatic, and stromal tumors. The discussion emphasizes the interplay between anatomical considerations and surgical demands, as well as the anesthetic implications of cancer-related physiological derangements such as cachexia, malnutrition, anemia, and immunosuppression.

A focused approach to preoperative optimization, including Enhanced Recovery After Surgery (ERAS) protocols and prehabilitation strategies, is presented alongside a detailed review of anesthetic techniques—ranging from total intravenous anesthesia (TIVA) to regional modalities—and pharmacological considerations unique to oncologic surgery. Procedure-specific challenges are analyzed in the context of esophagectomy, gastrectomy, hepatectomy, pancreaticoduodenectomy, and carcinoid tumor resection, with particular attention to fluid management, pain control, and intraoperative monitoring.

Additionally, the chapter addresses the growing evidence linking anesthetic management to long-term oncologic outcomes, including tumor recurrence and immune modulation. It concludes with a forward-looking discussion on emerging practices in immunomodulatory anesthesia, ERAS innovations, and the role of anesthesiology in optimizing return to intended oncologic therapy (RIOT). This chapter aims to serve as a practical and evidence-based reference for anesthesiologists managing patients with GI cancers in high-acuity surgical settings.

Keywords: Blood transfusion, Enhanced Recovery After Surgery (ERAS), GI oncology anesthesia, Multimodal analgesia, Opioid-sparing, Regional anesthesia.

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INTRODUCTION TO GASTROINTESTINAL ANESTHESIA

Gastrointestinal (GI) cancer surgeries present significant anesthetic challenges due to the complexity of the operations and the often fragile condition of oncology patients. These surgeries involve extensive anatomy – from the esophagus and stomach to the intestines, liver, and pancreas and may require large incisions, retraction, and occasionally thoracic components (*e.g.*, esophagectomies), all contributing to physiological stress. A thorough understanding of GI anatomy and tumor biology is essential, and anesthesiologists must be familiar with the anatomical considerations and clinical course of common GI malignancies (such as esophageal, gastric, colorectal, hepatobiliary, pancreatic cancers, and gastrointestinal stromal tumors) in order to optimally plan perioperative care [1]. GI tumors are among the leading causes of cancer morbidity, and their resection can be curative but is associated with high perioperative risk due to factors like tumor bleeding, nutritional derangements, and the potential for major fluid shifts or blood loss.

Patient-Specific Factors: Patients with GI cancers frequently present with cachexia, anemia, and malnutrition. Tumor-related anorexia and metabolic changes (cancer cachexia) lead to loss of lean body mass and hypoalbuminemia, which in turn alter drug pharmacokinetics and reduce physiologic reserve. Malnutrition is a well-known predictor of poor surgical outcomes; for example, in esophageal cancer surgery, poor preoperative nutritional status correlates with significantly higher postoperative complication rates [2]. Anemia is common (due to chronic blood loss or bone marrow suppression from cancer or chemotherapy) and can exacerbate tissue hypoxia; it should be optimized preoperatively (*e.g.*, with iron therapy or erythropoietin) to reduce the need for transfusions. Additionally, many cancer patients are immunosuppressed from the malignancy or prior treatments, increasing their infection risk. The anesthesiologist's preoperative assessment should thus include a careful evaluation of nutritional and volume status, end-organ function, and performance status. Often, a multidisciplinary optimization is needed, such as dietary counseling or feeding tube placement for severe malnutrition, or hematologic optimization for anemia.

Preoperative Risk Assessment and Optimization: Careful risk stratification is critical in GI oncology cases. Standard cardiopulmonary evaluation must be tailored to the patient's oncologic history – for instance, identifying cardiotoxic effects of chemotherapy or reduced pulmonary reserve from prior thoracic radiation. Objective measures like cardiopulmonary exercise testing or frailty indices can help quantify risk, aligning with the updated 2024 AHA Guidelines.

Optimization strategies are implemented whenever possible: treatment of anemia, aggressive nutritional support, physiotherapy for deconditioned patients, glycemic control in diabetics (pancreatic cancer patients may have diabetes), and abstinence from smoking and alcohol. Evidence suggests that interventions such as smoking cessation at least several weeks before surgery reduce postoperative pulmonary and wound complications [3]. In summary, the aim is to have the patient optimized as much as possible prior to undergoing these large operations.

Perioperative Goals: The overarching anesthetic goals for GI cancer surgery are maintaining hemodynamic stability, attenuating the surgical stress response, and providing effective analgesia (often *via* multimodal strategies) to facilitate recovery. Hemodynamic stability can be challenging to maintain during phases like induction (due to hypovolemia in dehydrated or bowel-prepped patients) or during large fluid shifts (*e.g.*, during liver resection or when the abdomen is open and exposed). Invasive arterial monitoring is commonly used for blood pressure management, and central venous access is often indicated for major cases for vasopressor infusions or rapid volume shifts. Close communication with the surgical team is important to anticipate stages of the operation that may require blood conservation (such as hepatic vascular clamping). Attenuating the surgical stress response is another key goal: major surgery triggers a surge of catecholamines and inflammatory cytokines, leading to immunosuppression in the perioperative period [4, 5].

This immunosuppressive (characterized by high levels of stress hormones and prostaglandins) can potentially promote tumor cell dissemination and impair wound healing [4]. Anesthetic techniques that blunt this response, such as epidural analgesia, regional blocks, and depth of anesthesia sufficient to prevent excessive sympathetic surges, are therefore desirable. Finally, multimodal analgesia, combining regional anesthesia, non-opioid analgesics, and other adjuncts to minimize opioid requirements, is very important. Effective pain control not only improves patient comfort but also enables early mobilization, deep breathing exercises, and faster return of bowel function, all of which are critical in ERAS (Enhanced Recovery After Surgery) protocols.

Preoperative Considerations in GI Oncology Surgery

Enhanced Recovery After Surgery (ERAS) Protocols: ERAS principles have become the standard of care in many GI oncology centers, with protocols specifically developed for colorectal, pancreatic, gastric, and esophagectomy surgeries. ERAS is a multimodal perioperative care pathway designed to reduce the surgical stress response and expedite recovery. Key ERAS elements begin preoperatively: patient education, optimization of medical comorbidities,

CHAPTER 16

Management and Treatment of Pain in Cancer Patients

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Abstract: Cancer pain is a complex condition that significantly impacts the quality of life in patients at all stages of disease. Effective pain management requires a nuanced understanding of the underlying causes of pain. This chapter provides a comprehensive review of cancer pain management strategies, with evidence-based approaches to assessment and treatment.

Keywords: Adjuvant analgesics, Breakthrough pain, Cancer pain, Chemotherapy-induced peripheral neuropathy, Cognitive-behavioral therapy, Epidural injections, Gene therapy, Intrathecal drug delivery, Interventional pain management, Multidisciplinary care.

INTRODUCTION

Pain secondary to malignancy is a prevalent symptom experienced by cancer patients. Chronic pain is defined as pain that persists or recurs for more than three months. Along with the distressing symptoms already faced by a cancer patient, pain on top can further exacerbate complications and the treatment process. It can arise at any stage of the disease, due to the tumor itself, treatments, or other medical factors related to the patient's condition. Effective pain management is essential for reducing suffering but also plays a crucial role in enhancing the patient's functional ability and psychological state. Despite advances in medical therapies, pain in cancer patients remains under-treated in many cases, often due to misconceptions about opioid use, inadequate assessment, or challenges in managing complex pain syndromes. It is important for the clinician to employ a comprehensive, multidisciplinary approach that includes both pharmacological and non-pharmacological methods to help optimize pain control and improve quality of life for cancer patients at every stage.

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Pathophysiology of Cancer Pain

Cancer pain arises from multiple mechanisms, each contributing to the complexity of pain perception in oncology patients [1]. Pain can be broadly classified into two main categories: 1. nociceptive pain and 2. neuropathic pain. The additional diagnosis of cancer leads to tumor and treatment-related factors, which also play a role [2].

Nociceptive pain is a type of pain that occurs due to tissue damage or inflammation, leading to activation of peripheral nociceptors that transmit pain signals throughout the nervous system [3]. Nociceptive pain can be broadly divided into two sources:

1. Somatic pain originates from bones, muscles, joints, or connective tissues. Somatic pain is well-localized and can be characterized as aching, sharp, or throbbing in nature and can often exacerbate with mobility. With regard to cancer pain, bone metastases can be a common cause [4].
2. Visceral pain originates from internal organs such as the intestines, liver, or pancreas. This pain is characterized as diffuse and dull and can be accompanied by referred pain. Tumors encapsulating the gastrointestinal tract or liver can lead to this type of pain [5].

Neuropathic pain occurs due to nerve damage, either due to the tumor itself or as a result of treatment [6]. It is characterized by burning, shooting, sharp, tingling, or electrical shock-like sensations. Nociceptive pain is usually more responsive to conventional analgesics as opposed to neuropathic pain [7]. A tumor can infiltrate the nerves, leading to direct compression and severe symptoms.

Cancer itself can be a source of pain, arising from various mechanisms [8].Tumors invade and compress nerves, bones, and soft tissues, leading to inflammatory and neuropathic pain. Metastatic disease due to the bone leads to pathologic fractures and inflammatory cytokine release [9]. Tumors can obstruct organs and tracts in the gastrointestinal and genitourinary system, causing colicky visceral pain secondary to distension [10]. Vascular compression from tumors induces ischemic pain. Metastatic disease from breast cancer, lung cancer, melanoma, and lymphoma can lead to Leptomeningeal carcinomatosis, a condition where infiltration of the meninges causes headaches, nausea, vomiting, as well as sensory and motor deficits [11].

Treatment modalities such as chemotherapy can induce chronic peripheral neuropathy [12]. Chemotherapy-induced peripheral neuropathy (CIPN) agents, such as platinum-based drugs, taxanes, and vinca alkaloids, are known culprits

that can damage peripheral nerves during treatment [13]. Furthermore, post-surgical nerve injury can introduce trauma in cancer-related surgeries, and Radiation-induced nerve damage can cause fibrosis and scarring, resulting in neuropathic pain syndromes [14]. The table below summarizes common causes of treatment-related pain (Table **1**).

Table 1. Common causes of cancer-treatment related pain.

Cause	Examples
Chemotherapy-related pain	Peripheral neuropathy (*e.g.*, platinum-based drugs, taxanes)
-	Mucositis and stomatitis (*e.g.*, methotrexate, fluorouracil)
-	Myalgia and arthralgia (*e.g.*, paclitaxel, aromatase inhibitors)
Radiation therapy-induced pain	Fibrosis and scarring cause chronic pain
-	Brachial plexopathy from radiation exposure in breast cancer
-	Osteoradionecrosis leading to bone pain
Surgical pain	Post-mastectomy pain syndrome
-	Phantom limb pain following amputation
-	Post-thoracotomy pain syndrome due to intercostal nerve damage

Effective cancer pain management involves a thorough understanding of these pathophysiological mechanisms, allowing clinicians to tailor multimodal treatment strategies that address the underlying cause of pain and improve patient outcomes [15]. Pain in cancer patients can be acute, chronic, or breakthrough pain. Acute pain arises immediately and is usually self-limited [16]. This can be secondary to acute post-operative surgical procedures or tumor growth. Chronic pain persists 3-6 months beyond the normal course of expected healing and can arise from cancer progression or treatment-related effects [17]. Breakthrough pain is a transient event that can result in intermittent exacerbations despite ongoing analgesia treatment [18].

Pain Assessment in Cancer Patients

A comprehensive pain assessment in cancer patients should include a detailed history and physical examination, a quantifying pain scale, psychological assessment, and pertinent diagnostic imaging to identify underlying causes and guide treatment [15].

History should include the character, onset, location, duration, intensity, exacerbation, and relieving factors [15]. Impact on activities of daily living (ADLs), level of function, and sleep must be documented. A patient's history of

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