34 Perioperative Complications in Oncosurgeries

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34.1 Introduction

Due to the considerable burden of cancer today, oncosurgeries are being performed at many centers globally and comprise a significant proportion of the hospital workload. As technology evolves, surgical procedures become more complex and intricate requiring very astute perioperative care. Many more cancer patients with multiple comorbidities are now offered these procedures than ever before, with either an intent to cure or for palliation, and this makes the perioperative management very challenging. Despite better facilities, expertise, and equipment, certain complications do occur and remain inevitable, though lesser in frequency. This is partly due to the inherent nature of the surgical procedures, which may be over long hours, may be technically tedious, and may involve two or more body compartments with the additional challenge quite often of an immune-compromised patient. Then, there is always a lack of desirable length of time for adequate optimization preoperatively as there is this intent to contain the disease as early as possible. Most of the oncosurgical units have well-defined protocols and standards of care and are always in a state of readiness to deal with complications arising in patients undergoing oncosurgery. This chapter reviews the various complications occurring in the perioperative period in patients undergoing oncosurgeries.

34.2 Perioperative Complications in Oncosurgeries

Various perioperative complications encountered in oncosurgeries have been reported in the literature. These can be broadly divided into general complications and complications specific to oncosurgical patients (Table 34.1). In this chapter, some surgical complications have been mentioned too as they pose a challenge to both surgeons and anesthesiologists involved in perioperative care.

A proactive approach by the multidisciplinary perioperative team is desirable for the care of oncosurgical patients to foresee complications and chart a course right from the beginning. Every step must be taken to optimize adverse factors and prevent complications or at the very least reduce the impact on the outcome. Return to intended oncological therapy (RIOT) is the goal, and all the efforts must be directed toward ensuring this endpoint.

In patients with colorectal cancer, postoperative complications after curative surgery had a negative impact on overall survival and cancer recurrence.

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Table 34.1 Perioperative complications in oncosurgeries

General complications in oncosurgery	Inadvertent perioperative hypothermia
	Deep vein thrombosis and pulmonary embolism
	Perioperative injuries
	Postoperative lung complications
	Sepsis
	Postoperative nausea and vomiting (PONV)
	Postoperative atrial fibrillation (POAF)
	Chronic postsurgical pain (CPSP)
Specific complications in oncosurgery	Chemotherapy-related perioperative complications
	Opioid dependence
	Malnutrition and hypoalbuminemia
	Difficult access to the airway (tumor, postradiation, extubation dilemma)
	Problems of brachytherapy (nonoperating room, anesthesia, and patient transport)
	Carotid blowout syndrome
	Flap necrosis
	Chyle leak

The authors have suggested that in the future phase III trials for adjuvant chemotherapy in colorectal cancer, surgical morbidity must be incorporated as a stratification factor [1]. In a retrospective study of 239 patients undergoing gastrectomy for gastric cancer, postoperative complications were found to adversely affect the overall survival as also the disease-free survival [2]. So, utmost planning and care are desirable to prevent the occurrence of perioperative complications.

34.3 General Perioperative Complications in Oncosurgeries

Various factors have been reported in the literature which is related to adverse outcomes after oncosurgeries. The factors in general are detailed in the following section.

34.3.1 Inadvertent Perioperative Hypothermia (IPH)

Inadvertent perioperative hypothermia (IPH) where the core body temperature falls below 36 °C is encountered commonly in perioperative patients and requires well-placed strategies for its management. The higher American Society of Anaesthesiologists (ASA) physical status, combined general and regional anesthesia, emergency surgeries, major or intermediate-risk surgeries, and low body mass index (BMI) are some of the risk factors for IPH [3].

Perioperative hypothermia is a harbinger of dreaded complications like coagulopathy, surgical site infections, adverse cardiac events (myocardial ischemia and ventricular tachycardia), and increased length of stay. Updated National Institute for Health and Care Excellence (NICE) guidelines 2016 for prevention of IPH has suggested several preoperative, intraoperative, and postoperative preventive measures. Patients should not be transferred to operation theatre and anaesthesia should not be induced until core temperature has been documented as more than 36 °C. Forced-air warming, prewarmed fluids (within 30 min of removal from the warming device), adjustment of operating room ambient temperature, monitoring of core temperature and appropriate titration of active warming, use of heat and moisture exchange (HME) filters, and continuity of care in the postoperative period are some of the recommendations in this guideline [4]. In a systemic review in which 18 studies were included, forced-air warming was found to increase thermal comfort, reduce cardiac morbidity, and decrease the incidence of shivering and wound infection as compared to alternate forms of warming [5].

It has been reported that in patients with invasive urinary bladder malignancy and undergoing radical cystectomy, the occurrence of intraoperative hypothermia was a significant prognostic marker for overall survival, though, in this study, the patients in the hypothermia group had poor performance status and advanced disease as compared to the normothermia group [6].

34.3.2 Deep Vein Thrombosis (DVT) and Pulmonary Embolism (PE)

DVT is another known complication in cancer patients. Acute PE can become life-threatening, and chronic pulmonary thromboembolism can have a significant impact on the quality of life. DVT and PE have a higher incidence in cancer patients as compared to noncancer patients undergoing surgical interventions. The guidelines published in CHEST in 2012 outline a well-researched management strategy to prevent DVT and PE in this group of patients [7]. But what is required is excellent communication between team members regarding the timing with regional anesthesia, interaction with co-administered anticoagulants, antiplatelet, or nonsteroidal anti-inflammatory drugs (NSAIDs), and a very close watch on surgical drains. Teams must be fully involved in the assessment of the risk of bleeding and perform a risk–benefit analysis every day. In the intraoperative and postoperative period, high alertness is required to detect this complication. Transesophageal echocardiography (TEE) can be used to evaluate the right heart function in the perioperative period. The hospital should have a robust PE/DVT protocol to detect and treat this life-threatening complication.

34.3.3 Perioperative Injuries

Perioperative injuries are unintentional injuries, which add to the postoperative morbidity, psychological distress, and have the potential for medico-legal concerns (Table 34.2). These injuries may be pressure ulcers, injury of muscles or tendons, and nerve injuries. Perioperative injuries may be related to either surgical factors or patient-related factors.

Table 34.2 Factors responsible for perioperative injuries

Surgical factors	Patient factors
Improper positioning Nerve injury (transection, pressure, stretching) Retractors [8, 9] Muscle and tendon injury (blood pressure cuffs, inadvertent pressure by the operating team, surgical mops, stretching)	Preexisting injuries Diabetes mellitus Hypertension Postchemotherapy Hypothermia Electrolyte imbalance

While positioning for surgical interventions and placement of surgical retractors, a fine balance is required so that the safety of the patient is ensured without obstructing surgical access and allowing adequate access to anesthesiologists. Patients undergoing oncosurgical procedures are more prone to these unintended harms as the surgeries are performed over a longer duration, some require wider surgical exposures, and there may be tissue insult due to prolonged unavoidable hypotension due to blood loss. Many of them may have had predisposing factors like preoperative chemotherapy, radiotherapy, and other comorbidities like diabetes or chronic renal insufficiency. Many assessment scales have been reported and validated for use for different injuries in the perioperative period. Braden scale is widely used for risk stratification of patients prone to pressure sores. This scoring is based on sensory perception, skin moisture, activity, mobility, nutritional status, and exposure to friction and shear. Assessment Scale for the Development of Injuries due to Surgical Positioning (ELPO version 2) incorporates seven factors namely "surgical position, duration of surgery, type of anesthesia, support surface, limb position, comorbidities, and patient age to assess the risk of perioperative injuries" [10].

Patients should be evaluated preoperatively for any preexisting injuries and predisposing factors for the occurrence of injuries. The assessment findings must be documented in the patient record and discussed with the patient as well. The informed consent must make a mention of these findings and the potential risk of injury must be explained. All care should be taken to prevent further exacerbation, and preventive strategies should be planned for the perioperative period. Postoperatively patients should be evaluated, any new finding should be documented, and appropriate steps should be taken to mitigate the harm.

The Amaerican Society of Anaesthesiologists (ASA) has published an updated practice advisory for the prevention of perioperative peripheral nerve injury in 2018 [11].

34.3.4 Postoperative Pulmonary Complications (PPC)

Postoperative pulmonary complications (PPCs) and its impact on mortality [12, 13] and the cost of care is well-recognized. There are several predisposing factors (Table 34.3), and some of them are amenable to optimization or modification before surgery [14]. Quite often, cancer patients lose out to ideal optimization as there is a resolve to operate as early as possible to contain the disease.

Table 34.3 Predisposing factors for postoperative pulmonary complications in cancer patients

Patient-specific factors	• Advanced age • Male sex • American Society of Anesthesiologist (ASA) physical status 3 or more • Malnutrition, hypoalbuminemia, anemia • Recovering chest infection • Preoperative sepsis • Impaired cognition • Obesity • Postchemotherapy • Depression • Poor cardiac reserve • Myelosuppression • Diabetes mellitus • Chronic liver disease • Chronic renal disease • Ascites
Procedure-specific factors	• Major surgery in the abdominal or thoracic cavity or involving both (e.g., esophagectomy) • Head and neck surgery (inability to cough) • Open surgeries (vs. minimally invasive surgery) • Multiple blood transfusions (acute lung injury) • Prolonged postoperative ventilator support • Emergent surgery (vs. elective procedure) • Redo surgeries • Surgical complication (postoperative pneumothorax, hemothorax, chyle leak, anastomotic leaks) • Use of nasogastric tube

The preventive strategies include optimization of all modifiable factors as much as achievable, pre- and postoperative physiotherapy and breathing exercises, acute pain management plan, and a low threshold for detecting infections. A preexisting plan or protocol is not sufficient. There must be frequent assessments for any such complication and its management at the earliest. The role of epidural analgesia in reducing the risk of postoperative pulmonary complications is well known [15, 16].

To reduce PPCs, a postoperative protocolized program based on patient education, early mobilization, and pulmonary interventions called “I COUGH” was found to appreciably reduce the incidence of postoperative pneumonia (from 2.6% to 1.6%) and unplanned intubation from 2% to 1.2% [17].

34.3.5 Perioperative Sepsis

Sepsis has been defined as “a life-threatening organ dysfunction caused by a dysregulated host response to infection.” The presence of an infection, abnormal regulation of the host response to the infection and the organ dysfunction occuring as a result of this abnormal response comprise three critical components of sepsis [18].

Sepsis is the cause of 9% of all cancer-related mortalities in the United States of America [19]. The operated cases of cancer are more prone to sepsis due to an immune deficiency state causing cancer [20, 21] and/or chemotherapy-related depressed immune status, lymphadenectomy performed during surgery, indwelling central venous lines, or urinary catheters, and blood transfusion-related immunomodulation (TRIM) [22]. All guidelines regarding the prevention of surgical site infection (SSIs), catheter-associated urinary tract infection (CAUTIs), and catheter-related bloodstream infections (CRBSIs) should be strictly followed. Healthcare workers involved in the care must follow all hand hygiene protocols and wear appropriate personal protection equipment.

A heightened vigilance should be maintained to detect signs and symptoms of sepsis, and there must be no delays in obtaining cultures from drains, surgical wounds, and bronchoalveolar lavage fluid. Sequential Organ Failure Assessment score (SOFA) can be used to identify organ failure.

In the Surviving Sepsis Guidelines 2016, the 3- and 6-h bundles focus on time-targeted measurement and monitoring of lactates, the institution of fluid boluses, obtaining blood cultures, focused reassessment, and initiation of vasopressors. Noradrenaline is the vasopressor of choice, and phenylephrine is no longer recommended. Within an hour of diagnosis, empirical broad-spectrum antimicrobials covering all likely pathogens, including bacteria and any potential viruses and/or fungi based on the risk factors in the patient, must be commenced. This can be tailored once the results of cultures become available. Blood glucose levels above 180 mg/dL should be treated with a target of <180 mg/dL, continuous renal replacement therapy is indicated over intermittent therapy in hemodynamically unstable patients, stress ulcers and DVT prophylaxis should be given, and enteral nutrition should be started as early as possible. In patients with feeding intolerance, the use of prokinetic agents and the placement of feeding tubes in a postpyloric position have been suggested in this guideline [23].

34.3.6 Postoperative Nausea and Vomiting

Postoperative nausea and vomiting (PONV) are among the most distressing concerns for any patient. Usually, patients present for surgery after a gap of a few weeks after chemotherapy; hence, chemotherapy-induced nausea and vomiting have mostly subsided by then.

Hypercalcemia, uremia, ascites, brain metastasis, medication, gastritis, intestinal obstruction, and anxiety may cause nausea and/or vomiting in an oncosurgical patient and may subside once the cause is addressed. Apart from these, intraoperative factors like the use of opioids, bowel handling and bowel paresis, gastritis, use of NSAIDs etc. have been related to the occurrence of PONV.

The class of drugs commonly used for treating PONV are 5HT3 receptor antagonists, steroids, antihistamines, and butyrophenones. Neurokinin 1 (NK1) receptor antagonists were discovered in the 1990s. The NK1 receptors are present centrally as well as peripherally, and this receptor has substance P as its natural ligand. Aprepitant is an NK1 receptor antagonist and is commercially available in several countries. It has been used in patients of debulking surgery undergoing postoperative intraperitoneal chemotherapy [24]. In a systemic review, aprepitant was found to reduce the incidence of vomiting on the first two postoperative days (some heterogenicity was noted) with minimum need for rescue on the first postoperative day and a dose of 80 mg was found to be effective and safe [25].

In 2014, Society for Ambulatory Anesthesia published a comprehensive guideline for the management of PONV listing the risk factors (female gender, nonsmoker, previous history of nausea and vomiting, emetogenic surgeries), the scoring system for patients at risk, preventive strategies, and the dose and timing of antiemetics [26]. The choice and combination of drugs depend on the risk factors.

34.3.7 Postoperative Atrial Fibrillation (POAF)

New-onset postoperative atrial fibrillation (POAF) is the most common cardiac arrhythmia seen in oncosurgical patients after major surgery. Many patients undergoing noncardiac surgery develop clinically significant atrial fibrillation (AF) [27], and the incidence was reported as 12.3% in 2588 patients undergoing thoracic surgery for benign and malignant conditions [28]. Though mostly self-limiting, it results in a considerable increase in the cost of care, prolonged length of stay, and significant morbidity. Thromboembolic event is the most dreaded consequence of AF as it can cause a stroke or acute limb ischemia.

The American Association of Thoracic Surgeons (AATS) 2014 guidelines for the prevention and management of perioperative atrial fibrillation and flutter for thoracic surgical procedures [29] has laid down definitions for the diagnosis of POAF following thoracic surgery. The AATS defines *electrophysiologic definition/diagnosis* as “ECG recordings (1 or more ECG leads)with ECG features of AF lasting at least for 30 seconds or the duration of the ECG (<30 s)” and *clinical definition/diagnosis* as “clinically significant POAF is intra- and postoperative AF requiring treatment, or anticoagulation, and/or extending the duration of hospitalization” [29].

Additionally, they have identified modifiable and nonmodifiable risk factors (Table 34.4) for POAF based on the American Heart Association Atrial Fibrillation guidelines and relevant literature on thoracic surgery. In this publication, thoracic surgical procedures have been divided into low-risk (5%), moderate-risk (5–15%), and high-risk (9.15%) categories based on their expected incidence of POAF.

For patients undergoing surgical interventions having high risk (>15%) of incidence of AF intermediate (5–15%) risk for POAF, a continuous ECG monitoring is suggested postoperatively for 72 h (or less if their shorter length of stay). This recommendation should also be followed in patients with significant additional risk factors (CHA2DS2-VASc > 2) for stroke or with a history of preexisting or periodic recurrent AF before their surgery. ECG monitoring must be continued in the postoperative period for patients who have received epidural catheters and regional anesthesia blocks, and similar are performed [29].

Table 34.4 Risk factors for postoperative atrial fibrillation

Modifiable risk factors	Nonmodifiable risk factors
Hypertension Myocardial infarction Valvular heart disease History of heart failure Obese Obstructive sleep apnea Chronic smoker Exercise Alcohol consumption Hyperthyroidism Increased pulse pressure Mitral regurgitation Left ventricular hypertrophy Increased left ventricular wall thickness	Age Genetic variants Race – African American Family history Male History of arrhythmias

The pharmacological control of heart rate in patients with AF is desirable. Various drugs have been suggested, and beta-blockers remain the drug of choice for control of rapid ventricular rate in patients with AF. Alternately, nondihydropyridine calcium channel blockers may be used in case beta-blockers are contraindicated like in patients with reactive airway disease. These drugs need to be used cautiously in patients with systolic heart failure. In such situations or when the response to these drugs is not optimal, amiodarone may be alternatively used. For patients with low left ventricular ejection fraction, the use of digoxin with beta-blocker or a calcium channel blocker may be administered to control the ventricular heart rate. Since postoperative patients have a high sympathetic tone, digoxin as a sole agent should not be used [30].

To mitigate the risk of thromboembolism, it is reasonable to initiate anticoagulation in patients in whom AF has persisted for 48 h or more. A CHADS2 score or CHA2DS2VASc score of 2 or more mandates the use of anticoagulants [31, 32]. Also, an appropriate risk–benefit analysis must be done to weigh the benefits of anticoagulation with the risk of postoperative bleeding. Toward this, HAS-BLED (hypertension, abnormal renal/liver function, stroke, bleeding history, or predisposition, labile INR, elderly, drugs/alcohol concomitantly) score can be calculated [33]. While making these decisions, it is of paramount importance that these measures and their implications are discussed and explained to the patient and the caregivers.

34.3.8 Chronic Postsurgical Pain (CPSP)

This is a well-known entity after any major or minor surgery, not necessarily oncosurgeries, and a high incidence of CPSP has been reported after breast surgery, amputations, and thoracic surgeries [34]. CPSP was defined based on the duration of pain, the association with a surgical procedure, and the exclusion of other causes [34]. The CPSP definition proposed by Macrae (2001) was "pain should have developed after a surgical procedure; pain should be of at least 2 months' duration; other causes for the pain should be excluded, e.g. continuing malignancy (after surgery for cancer) or chronic infection; and in particular, the possibility that the pain is continuing from a pre-existing problem should be explored and exclusion attempted" [34]. It was redefined by Werner and Kongsgaard (2014) as "pain develops after a surgical procedure or increases in intensity after the surgical procedure; pain should be of at least 3–6 months' duration and significantly affect the quality of life; pain is either a continuation of acute post-surgery pain or develops after an asymptomatic period; pain is either localized to the surgical field, projected to the innervation territory of a nerve situated in the surgical field, or referred to a dermatome; and other causes of the pain should be excluded, e.g. infection, or continuing malignancy in cancer surgery" [35].

CPSP has a significant impact on the quality of life and increases the cost of medical care. The development of CPSP is multifactorial and can be broadly divided into nonmodifiable and modifiable factors (Table 34.5). Modifiable factors should be addressed as part of a well-planned perioperative strategy.

The role of preoperative counseling and allaying of anxiety and fear cannot be overemphasized. It has been reported that patients with a surgical outcome-related fear preoperatively have more pain, poor global recovery, and poorer quality of life after the surgical intervention as compared with patients who have an optimistic approach [36]. This aspect can be addressed with good preoperative counseling.

Table 34.5 Risk factors for chronic postsurgical pain

Nonmodifiable factors	Modifiable factors
Genetic predisposition Gender	Psychological factors Preemptive analgesia Better surgical techniques Shorter operating time Avoidance of nerve injury (cutting, stretching, crushing of nerves) Acute postoperative pain management

Laparoscopic surgeries offer an advantage as there is markedly reduced muscle injury and use of retractors; however, the incidence of post-thoracotomy pain syndrome was reported to be 25% after video-assisted thoracic surgery in a questionnaire-based study [37].

Better surgical skills can go a long way in reducing the incidence of CPSP. Breast surgery patients in a high-volume center are less likely to suffer from chronic pain, strange sensations in the ipsilateral arm, and phantom sensations in the removed breast, and this is due to higher surgical skills [38]. It is important to block or limit persistent pain sensitization in the postoperative period, and this requires newer therapies like multimodal pharmacological approaches. Future options like anti-nerve growth factor and Nav 1.7 antagonists to restore endogenous analgesia need to be explored [39].

34.4 Specific Perioperative Complications in Oncosurgeries

The oncosurgical interventions have some distinct complications that remain associated with patients with cancer. These specific cancer surgeries related complications are being discussed in the subsequent section.

34.4.1 Chemotherapy- and Radiotherapy-Related Perioperative Complications

The toxicity of chemotherapeutic agents can adversely impact cardiovascular, pulmonary, renal, hepatic, hemopoietic, and both central and peripheral nervous systems. There is a gap of about 3 weeks between neoadjuvant chemotherapy and surgery unless preoperative radiation has been given too wherein the gap may be as long as 10–12 weeks. All post-chemotherapy patients planned for surgery are high-risk patients. A thorough evaluation and optimization of chemotherapy-related side effects must be done preoperatively. The number of such patients has risen in the last decade and a half due to the increasing use of neoadjuvant chemotherapy.

There must be all-time heightened awareness in the postoperative period for existing as well as hibernating chemotherapy-related issues (Table 34.6) and a well-chalked out plan to preempt any further deterioration in the affected organ system.

Apart from the hepatotoxic effects of chemotherapy agents, liver injury secondary to radiation therapy is well documented. The patients present within 4 months following hepatic radia-

Table 34.6 Adverse effect of chemotherapeutic agents and management in the postoperative period

Organs affected	Chemotherapeutic agents	Adverse effects	Suggested management
Cardiotoxicity [40, 41]	Anthracyclines Anthraquinolones	Congestive heart failure Left ventricular dysfunction Acute myocarditis Arrhythmia	General physical examination, preoperative ECG, evaluation of left ventricular ejection fraction by a 2D echo, stress echo if required, baseline B-type natriuretic peptide, and troponins Involvement of cardiologists as part of a multidisciplinary perioperative team Cardioprotection with ACE inhibitors, angiotensin II receptor blockers, and β-blockers may be considered Prophylaxis for thromboembolism after risk–benefit analysis
	Capecitabine 5-fluorouracil Cytarabine	Congestive heart failure and cardiogenic shock Myocardial ischemia Pericarditis	
	Paclitaxel Vinca alkaloids	Congestive heart failure Myocardial ischemia Hypotension Rhythms disturbances—block (atrioventricular, ventricular tachycardia, sinus bradycardia)	
	Cyclophosphamide	Valvular dysfunction—mitral regurgitation Neurohumoral activation	
	Imatinib	Congestive heart failure Left ventricular dysfunction arrhythmias Angioedema	
	Ifosfamide Gemcitabine Melphalan Cisplatin Docetaxel 5-fluorouracil Etoposide High doses of corticosteroid	Atrial fibrillation	
Hepatotoxicity [42–47]	Irinotecan	Steatohepatitis	Baseline liver functions and a close watch in the postoperative period Tests for assessing hepatic clearance of compounds like indocyanine green Imaging for residual liver remnant after hepatectomy Optimal recovery of the functional status of the organ system (5 weeks) [46, 47]
	Oxaliplatin	Sinusoidal dilation Vascular lesions requiring increased blood transfusion	
	Tamoxifen	Nonalcoholic fatty liver disease (NAFLD) Nonalcoholic steatohepatitis (NASH)	
	Methotrexate	Cirrhosis	

Table 34.6 (continued)

Organs affected	Chemotherapeutic agents	Adverse effects	Suggested management
Nephrotoxicity	Cisplatin Ifosfamide Mithramycin	Acute tubular necrosis	Preoperative evaluation of renal function, watchfulness in female patients, diabetics, age > 65 years, preexisting chronic renal disease Prevention of volume depletion and renal hypoperfusion Avoidance of nephrotoxic agents
	Methotrexate	Crystal nephropathy	
	Bevacizumab Tyrosine kinase inhibitors Mitomycin Gemcitabine	Thrombotic microangiopathy	
	IFN Pamidronate	Focal segmental glomerulosclerosis	
	Sorafenib Sunitinib	Acute interstitial nephritis	
Toxicity of central and peripheral and autonomic nervous system [48, 49]	Paclitaxel	Demyelination	Identification and documentation Measures to prevent postoperative cognitive dysfunction, assisted mobilization, prevention of falls, prevention of position-related injuries and pressure sores in the perioperative period with frequent changing of postures and padding Matching any deficit with the preoperative mapped areas
	Vinca alkaloids	Loss of deep tendon reflexes, numbness, and burning sensation in hand and feet Orthostatic hypotension Myalgia Loss of pain and temperature sensation	
	Cisplatin	Loss of deep tendon reflexes, ototoxicity, sensory ataxia	
	Ifosfamide	Somnolence, confusion, dizziness, cranial nerve dysfunction, depressive psychosis, seizures, coma	
	Methotrexate	Headache, lethargy, nuchal rigidity, cerebellar dysfunction	
	Oxaliplatin	Acute sensory symptoms and chronic sensory neuropathy	
	Bortezomib	Painful, small fiber sensory neuropathy	

tion therapy with classic symptoms of radiation-induced liver disease (RILD). These symptoms include ascites without icterus, hepatomegaly, and isolated disproportionate elevation of alkaline phosphatase. The same level of derangement is not seen in other liver enzymes. Patients with preexisting liver disease are more susceptible, and they may manifest as nonclassic RILD.

Radioembolization-induced liver disease (REILD) is also a recognized adverse effect of cancer-related therapy. It appears 4–8 weeks following radioembolization treatment for cancer and pathologically leads to sinusoidal obstruction syndrome. Patient presents with symptoms like jaundice and ascites with increasing levels of gamma-glutamyl transpeptidase (GGTP) and alkaline phosphatase [50]. Chemotherapeutic agents may injure vasculature of the kidney, glomerulus, proximal or distal tubules, and collecting ducts, and they may be classified accordingly [51].

It has been reported in a cross-sectional analysis of prospectively collected data from

3558 patients that the rate of acute kidney injury (AKI) in hospitalized cancer patients was much higher than those not suffering from cancer. Furthermore, irrespective of underlying cancer, those with diabetes and hyponatremia, on antibiotics and chemotherapy, with exposure to intravenous contrast, or with the history of ICU stay during hospital admission were at a higher risk for developing AKI in the hospital. There exist other several predisposing factors for AKI in cancer patients along with chemotherapy, and preemptive steps to prevent AKI may improve the clinical outcome [52].

While evaluating the patient for chemotherapy-related adverse effects on the central and peripheral nervous system, one must keep in mind other differential diagnoses like preexisting diabetic neuropathy, dementia, Vitamin B12 deficiency, Charcot–Marie–Tooth disease, peripheral vascular disease, and any paraneoplastic neuropathy like POEMS (Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal gammopathy, and Skin changes). Any preexisting neuropathy should be mapped. Regional anesthesia should be avoided, or appropriate informed consent must be taken.

34.4.2 Challenges of Chronic Opioid Therapy

Management of anesthesia and postoperative pain can pose a challenge in cancer patients on chronic opioid use who are scheduled for palliative procedures. Unlike patients with addiction to recreational agents, the patient knows the drug and dosages, or his caregiver has all the details. These drugs are mostly according to the national health regulations in their country, and there is a prescription available.

The routine dose of analgesics that a patient is taking for his pain management needs to be continued until the day of surgery. A patient on pure μ agonist should not be shifted to a partial agonist or an agonist–antagonist. In India, morphine is the most prescribed opioid in cancer patients. Baseline opioid requirements should be met with an additional dosages of the same, or another short-acting pure mu agonist opioid can be added for acute pain in the perioperative period. As the acute pain following surgery subsides, these can be gradually reduced, and patients can then continue with the earlier or newly tailored opioid dose. Additionally, paracetamol and nonsteroidal anti-inflammatory drugs (NSAIDs) remain an important component of multimodal management. Regional anesthesia can be given safely if there are no other contraindications. Other side effects of chronic opioid use like constipation, nausea, and cognitive impairment should be managed in the postoperative period.

34.4.3 Malnutrition, Hypoalbuminemia, and Anemia

Nutritional status is one of the important factors for an optimal perioperative outcome in oncosurgeries. Malnutrition has been reported to impact adversely the outcome parameters like morbidity, mortality, length of the hospital, and intensive care unit stay [53]. Hypoalbuminemia is one of the independent predictors for poor outcomes in oncosurgeries and is associated with an increased risk of deep vein thrombosis [54], surgical site infection [55], and nonhealing enteric fistula [56, 57]. Type, site of cancer, stage of cancer, apathy due to depression, and gastrointestinal side effects of preoperative radiation or chemotherapy can attribute to malnutrition. Patients undergoing palliative procedures may present with cachexia or sarcopenia.

Serum albumin levels correlated directly with perioperative morbidity and mortality. The mortality rate increases from less than 1% to 29% and morbidity rates increase from 10% to 65% when the serum albumin levels fall from greater than 46 g/L to less than 21 g/L in a cohort of patients scheduled for noncardiac surgeries. So, albumin may be considered one of the important perioperative predictors even in oncosurgeries. This prognostic tool is low cost, is easily available, and predicts accurately [58].

There are three key recommendations of the expert group of the European Society of

Parenteral and Enteral Nutrition (ESPN) [59]. The patients undergoing oncosurgeries should be screened for nutrition in the preoperative assessment irrespective of baseline BMI and weight. These assessments must be expanded to include body composition, anorexia, inflammatory biomarkers, physical function, and resting energy expenditure. The nutritional optimization should be initiated at the earliest. There must be individualized plans using multimodal interventions and should include appropriate planning and counseling for nutritional intake, physical activity, decreasing inflammation, and hypermetabolic stress [59]. The process must start as part of prehabilitation before surgery and continue during the perioperative period.

As per recommendations of ESPN guidelines on clinical nutrition in surgery in patients with poor nutritional risk, a wait of 7–14 days is appropriate even in cancer surgeries for nutritional therapy. The nutritional management should be initiated at the appropriate time in the preoperative period and should continue at the earliest after the surgery. It should be according to the tolerance of the patients, and the type of surgery and caution must be exercised with elderly patients. The selection of a route for nutrition needs to be selected as appropriate with preference enteral or oral route. Where enteral nutrition is contraindicated or not feasible or not tolerated, then parenteral nutrition should be instituted. In malnourished patients undergoing major upper gastrointestinal and pancreatic surgery, feeding through the nasojejunal tube or a feeding jejunostomy should be considered. If the requirement of tube feeding is longer than 4 weeks, then percutaneous endoscopic gastrostomy should be considered for optimal nutrition [60]. The combination of enteral with parenteral nutrition was found to be beneficial in elderly patients undergoing surgery for gastrointestinal malignancies [61].

Anemia in cancer patients may be due to malignancy-related blood loss, marrow infiltration, myelosuppression due to radiation or chemotherapy, poor intake, or chemotherapy-related chronic renal disease. Iron deficiency is one of the etiological reasons for anemia in cancer patients. Hence, assessment for the type of anemia in cancer patients should be done. Serum ferritin, C-reactive protein, and transferrin saturation aid in making a diagnosis of anemia. Of these, serum ferritin level < 30 μg/L has been recognized to be diagnostic for diagnosing iron deficiency anemia. Other markers like the levels of C-reactive protein>5 mg/L and/or transferrin saturation < 20% with a serum ferritin level < 100 μg/L indicated toward the diagnosis of iron deficiency anemia. If surgery is scheduled in less than 6 weeks, then parenteral iron should be given, but if surgery is 6–8 weeks later, then oral iron supplements and nutrition should be given for the management of anemia [62, 63]. Erythropoietin is used in treating anemia due to myelosuppression, but the threat of deep vein thrombosis should be kept in mind.

34.4.4 Difficult Airway

Cancers of head and neck (H&N) are a significant proportion of overall malignancy worldwide, and difficult airway remains challenging in these patients. These difficult airways comprise over 75% wherein difficulty in maintaining oxygenation or complete ventilation failure remains a possibility and mandates the needs of surgical access [64–66].

Apart from an infiltrating tumor, radiation renders tracheal intubation and mask ventilation difficult by causing tissue fibrosis, loss of tissue compliance, restricted mouth opening and neck extension, and glottic and epiglottic edema [67]. History suggestive of difficult airway is one of the important indicators of present difficult airway, but caution should be taken even if this was suggestive of a normal/easy airway [68]. Patients with H&N pathology have a high incidence of difficult video laryngoscopy than other patients. The strongest predictors of Glide Scope failure were conditions that are likely to exist in H&N cancer patients, including prior neck radiation, abnormal neck anatomy, and airway masses [69].

In advanced H&N disease, even a surgical airway becomes very challenging and sometimes impossible due to decreased mandibular protrusion and postradiation changes in the neck. A successful airway strategy requires a preformulated plan for managing failed intubation attempts and for achieving and maintaining adequate ventilation, oxygenation, and protection against aspiration [70]. The optimal airway management approach depends on the surgical procedure, location of the lesion, patient symptoms, acuity of the situation, and the patient's tolerance of the airway management procedure. It may also be dictated by the anesthesiologist's skill set and equipment availability.

H&N tumors can cause airway distortion and can be friable, leading to bleeding, fragmentation, airway soiling, and rapid edema formation with laryngoscopy. Due to this, airway access may deteriorate even after a single aborted attempt and may worsen with repeated attempts at direct laryngoscopy in these patients. If direct laryngoscopy (DL) is chosen as a primary approach to tracheal intubation, multiple attempts should be avoided to avert total airway obstruction. The use of a flexible endoscope or video laryngoscope needs to be considered as a choice of equipment in patients with H&N cancers. At times, the use of a rigid bronchoscope remains a rescue measure especially in conditions of airway obstruction due to tumor mass, bleeding, etc. [71, 72]. The most common reasons for the failure of flexible scope tracheal intubation in these patients include the inability to identify the glottis, difficulty in passing the scope, bleeding, and airway obstruction [65]. Optical intubation stylets may have some advantages over flexible scopes. These rigid devices may bypass mobile supraglottic and glottic masses in situations when a flexible scope will not pass. Supraglottic airway devices may be difficult to insert or seat in patients with H&N pathology due to abnormal anatomy. History of neck radiation; limited mouth opening; and glottic, hypopharyngeal, and subglottic pathology, all of which may be present in these patients, are predictors of difficulty with supraglottic airway ventilation.

The combined use of video laryngoscopy with a flexible scope or optical stylet is increasingly common in complex airway management. Video laryngoscopy provides a clear view of the glottis and thus allows negotiation of the flexible scope or optical stylet in patients with distorted anatomy or airway tumors. The combined technique is thus useful for not only providing clear images but also providing dynamic images for observing the real-time intubation procedures and preventing any direct trauma to the mass lesion.

Oxygenation-centered airway management is critical for H&N cancer patients, who present with a higher incidence of failed tracheal intubation and "cannot intubate, cannot ventilate" (CICV) or complete ventilation failure situations. The use of high-flow nasal oxygen (transnasal humidified rapid insufflation ventilatory exchange [THRIVE]) is a useful technique and provides increased apnea time. The oxygenation throughout the intubation procedure remains an important step [73]. In selected cases, the use of transtracheal jet ventilation (TTJV) catheter or cannula or high-frequency TTJV [74] may be considered for preoxygenation before induction.

A tracheostomy may be planned as the primary intubation strategy for patients who are expected to have significant airway compromise after surgery. Most H&N cancer surgeons prefer to perform tracheostomies under controlled conditions, after induction of anesthesia, to avoid airway trauma, tumor disturbance, and tracheostomy tube displacement or obstruction. The final decision is usually taken in a controlled environment after the induction of anesthesia. In case, awake surgical access is deemed necessary, then a difficult airway cart should be ready and avoid any sedation. An awake dilator cricothyroidotomy is another good alternative [75]. For emergency airway management, surgical cricothyroidotomy is strongly preferred over percutaneous access through the cricothyroid membrane.

Inhalation induction should be considered for patients with H&N cancer only after consultation with the surgeon and evaluation of the predicted difficulty with mask ventilation and may be best reserved for patients with noncollapsing lesions [76]. Inhalation induction may be highly problematic for patients with difficult mask ventilation.

Emergence from anesthesia for H&N cancer patients should include a smooth, rapid awakening and extubation. Extubation should be devoid of coughing, bucking, and straining. Blood pressure should be controlled during emergence and in the immediate postoperative period for many H&N procedures.

Endotracheal extubation should be planned as thoroughly as endotracheal intubation and requires a strategy for patients who undergo H&N procedures.

Compared with other elective surgeries, H&N surgeries are associated with higher rates of airway complications like laryngospasm, postextubation airway edema, postoperative airway obstruction, and need for reintubation during and immediately after emergence and well-planned extubation [77]. One-third of adverse events reported to the fourth National Audit Project (NAP) of the Royal College of Anaesthetists occurred during emergence and recovery from anesthesia [78]. The plan for extubation should be formulated with the surgeon and should consider the difficulty of initial intubation, the extent and duration of surgery, the potential for postoperative swelling or bleeding, and the patient's current and preoperative medical status. The algorithm of the Difficult Airway Society (DAS) and All India Difficult Airway Association (AIDAA) can be a good foundation for the extubation strategy. The use of a supraglottic airway device as a primary ventilatory device, instead of an endotracheal tube for smooth emergence and extubation (Bailey Maneuver), is a well-known strategy [79]. Extubation can be delayed in cases of anticipated extubation failure. Such patients must be managed in an intensive care setting allowing 24–48 hours for the surgical edema to subside. Thereafter extubation should be carried out under the supervision of personnel with expertise in airway management and with a difficult airway cart at bedside. The use of bridge adjuncts like airway exchange catheter remains useful.

34.4.5 Problems of Brachytherapy and Intraoperative Radiation

Brachytherapy is one of the modalities to provide radiation therapy and is being used for H&N cancers as well. Here, the catheters are placed at the site of cancer lesion at suitable distances and radiation is provided using these brachy-catheters. This technique provides radiation exposure to the cancer lesion without having adverse effects on other nearby structures even at high doses [80].

Advanced head and neck tumors and tumors of the pelvis and retroperitoneum may require intraoperative radiation therapy (IORT). After debulking of the tumor, the nearby normal vital organs/structures are manually moved out of the way and protected with the shield. The patient is then shifted from the operation room to the brachytherapy suite, and here, a high dose of radiation as per calculations is directed onto the target surface.

IORT necessitates the continuation of anesthesia care beyond the familiar operating room setup to a remote area. The patient is shifted to the brachytherapy suite while maintaining anesthesia with intravenous agents like propofol and opioids. Manual ventilation or portable ventilators are used if neuromuscular blocking agents are used. An anesthesiologist always accompanies the patient maintaining the standards of care and monitoring. The American Society of Anesthesiologists (ASA) guidelines for providing anesthesia in the nonoperating room must be followed [81]. The location should have an anesthesia machine with drugs and standard monitors, a resuscitation cart with the defibrillator and emergency drugs, a source of oxygen, suction, anesthesia gas scavenging, and trained support staff.

The radiation equipment is maintained at a low temperature to prevent overheating. Hence, it is important to maintain normothermia in anesthetized patients with warming blankets and warm intravenous fluids. Considering that levels of radiation in the brachytherapy suite are very high, the staff must be protected with lead aprons and thyroid shields [82].

To prevent radiation exposure-related health hazards, the anesthesiologist should not be present during radiation therapy. A remote-controlled duplicate set of monitors (master and slave concept) should be available outside the radiation area. Video cameras should be installed so that the patient can be monitored for any movement, displacement of the endotracheal tube, invasive lines, or intravenous connections. There should be a provision to stop the radiation immediately if patient safety is compromised due to any reason.

34.4.6 Carotid Blow Out Syndrome

Carotid blow out syndrome (CBS) is one of the complications seen in patients undergoing cancer treatment (surgery and radiotherapy), especially for H&N cancers. It has been observed in around 3–5% of such patients [83]. The presentation is sudden massive trans-oral or trans-cervical bleeding with high rates of mortality and neurological morbidity.

CBS may present in three different clinical conditions depending on the severity. CBS may present with threatened blowout where vessels are clinically exposed or there is the invasion of vessels by the tumor as evident from imaging modalities. CBS may also be evident as an impending blowout where the bleeding from the vessel has stopped spontaneously. The most dreaded CBS presentation is acute, profuse, and uncontrollable bleeding [84].

The gold standard modality for diagnosis of CBS is angiography. This technique also provided therapeutic options simultaneously like endovascular stenting [85]. Computed tomographic and magnetic resonance angiography can also be used to identify the threatened lesions [86].

Early endovascular stenting is indicated in threatened lesions to prevent hemorrhage. But an impending or acute CBS requires volume resuscitation, application of pressure to stop the bleed, and earliest control of the airway. In successfully resuscitated and stabilized patients, endovascular procedures may be attempted. However, if interventional radiology therapies are unavailable or fail, then urgent surgical intervention is required. Suggested steps in the management of CBS include comprehensive management (Table 34.7).

In terminally ill patients with H&N cancers, if CBS appears to be likely, then an informed discussion must be held with the patient and the caregivers to plan the care and interventions. The wishes of the patient should be respected and care must focus on ensuring alleviation of symptoms and not prolongation of life.

Table 34.7 Suggested steps in the management of CBS

Pressure on the bleeding vessels using digital pressure or balloon tamponade
Initiate advanced trauma support protocol
Initiate massive transfusion protocol
Maintain oxygen saturation > 95%
Shift to operation room/endo-radiology suit
Surgical intervention includes debridement of the wound, excision of the malignant mass, closure of the fistula, coverage of the exposed vessel, and surgical site using a well-vascularized tissue graft.

34.4.7 Microvascular Flap Necrosis

The flap reconstruction is one of the important reconstructive aspects after H&N surgeries. These flaps could be either a free flap (microvascular flap) or a pedicle flap. These surgeries are frequently performed as part of cancer surgery for covering a resected area for functionality, protection, aesthetics, or a combination [87, 88]. The flap needs to be monitored in the postoperative period as flap loss remains a dreaded complication. Certain comorbidities in a patient and some perioperative conditions may predispose a patient to loss of a flap. Some of the risk factors considered to be responsible for flap necrosis are listed in Table 34.8.

The use of anticoagulants is one of the preventive measures, but no single anticoagulation regimen has been found to offer any significant advantage over others with regard to flap outcome including flap thrombosis and its loss [98]. The choice of anesthetic technique also has a role in the flap outcome. The principal goals in the perioperative period remain maintenance of low blood viscosity to maintain flap perfusion, better oxygenation, and vasodilation and maintain good perfusion pressure. The measures are required to prevent excessive blood loss during surgical resection. Balanced general anesthesia

Table 34.8 Patient and perioperative risk factors, which may result in flap necrosis

Patient risk factors	Perioperative risk factors
• Preoperative radiation [89] • ASA physical status III and higher [90, 91] • Age > 70 years [92] • Hypercoagulability (hereditary or acquired) [93] • Low cardiac output state, congestive cardiac failure, moderate-to-severe aortic stenosis, low cardiac index [94] • Preoperative anemia (<10 g/dL) [95]	• The length of the flap may lead to its kinking leading to compromised vascular supply and thus necrosis. Also, vessel compression, pedicle tension, external compression due to bandage, hematoma, neck position, etc. may lead to flap compromise [96] • Undetected ischemia of the flap • Hypotension • Prolonged surgical time [97]

with optimal vasodilation and minimal cardiac depression should be targeted during prolonged free flap procedures [99]. The use of regional blocks has been reported to be beneficial by vasodilation of the vessels, reduce vasospasm episodes of the grafted vessels, and thus maintain perfusion of the grafted flap. However, this has a limited role on H&N flap but good analgesia needs to be provided. Nonsteroidal anti-inflammatory drugs can increase the risk of perioperative bleeding and hematoma formation, and this effect may get potentiated in the presence of anticoagulation; hence, they should be avoided.

To avoid flap edema, crystalloids should be targeted to meet the basic physiological needs and its overloading should be avoided. The use of synthetic colloids is the other option to replace blood loss and maintain adequate tissue perfusion. Hematocrit and hemoglobin must be maintained with blood products to its physiological levels to maintain not only perfusion but also oxygenation. The vasopressors should be cautiously used, especially during the graft harvesting as vasopressors affect the vessel dimensions including perforators and its identification. This leads to the technical dissection of the flap with its blood supply [100]. Intraoperative hypothermia should be prevented by using fluid warmers and warm air systems.

34.4.8 Chyle Leak and Its Management

Chyle leak is an infrequent complication but it must be dealt with efficiently. In case it is leaking inside the chest or abdomen and not draining out then to prevent lung compromise, a chest tube insertion, repositioning of an existing one or a pigtail drain insertion, may be required. Most of these leaks resolve spontaneously though occasionally surgical intervention may be required. The main aim of the management of chyle leaks is to follow strategies that aid in decreasing the production of chyle itself. This shall in turn help in decreasing the ascites and pleural effusion, maintain fluid and electrolyte balance, and also prevent nutritional loss. Though there is no robust evidence, restricting lipids in the diet is widely practiced and the use of medium-chain triglycerides in enteral nutrition is encouraged [101].

34.5 Summary

The most effective step to prevent complications in oncosurgery is to keep all the complications on our clinical radar, ensure early detection, and prompt targeted treatment.

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