Onco-Critical Care

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32.1 Introduction

Over recent years, there have been several advancements in the early diagnosis and management of cancer. With a better understanding of disease pathologies and better chemotherapy, the overall five-year survival has improved significantly [1]. The intensive care unit (ICU) survival rates in both solid tumor and hematologic malignancies also have significantly improved from 15% to 50% over the recent years despite admitting sicker patients [2–5]. Oncology intensive care has contributed significantly to vital organ support among patients with cancer and treatment-related complications. Earlier considered as a futile attempt, now oncology critical care can be rewarding, with reduced mortality rates and substantial 5-year survival rates, especially if the intensivist can recognize the potentially curable critical illness among cancer patients [6].

32.2 Patient Admission into Oncology Critical Care

The common indications for ICU admission in oncology are outlined in Table 32.1 [7]. All critically ill patients with a reasonable prospect of recovery from their current illness or ailments should be offered critical care support abiding by the basic ethical principles, namely, beneficence, nonmaleficence, autonomy, and social justice [8]. Patients with aggressive malignancies resistant to treatment or in advanced stages of malignancy where the only option remains palliation of symptoms should not be admitted to ICU [9, 10]. Similarly, patients with aggressive graft-versus-host-disease (GVHD), reduced cancer-related life-expectancy (<1 year), and patients with poor performance score within the last 3 months before the precipitating event should not receive aggressive ICU therapies [11].

For those patients in whom the disease control is modest but has a probable control of disease, ICU admission may be considered on a case-by-case basis [12, 13]. Unduly delayed ICU admission may be associated with increased mortality in critically ill cancer patients [14, 15]. Existing screening tools have poor sensitivity and specificity to identify critically ill cancer patients who may benefit from early admission to critical care units [16, 17]. The development of a rapid response team combined with the use of predictive scoring systems and biomarkers such as lactate has proven to be effective in enhancing prompt admission to the ICU but needs further validation [18]. In the absence of accurate prediction systems, the current strategy of ICU admission for the majority of patients is that of a time-limited ICU trial admission. The various

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Table 32.1 Common indications for ICU admission in cancer patients

Medical emergencies unrelated to malignancy	Sepsis and septic shock, diabetic ketoacidosis, dyselectrolytemia, acute respiratory failure, acute myocardial infarction, pulmonary embolism, stroke
Exacerbations of pre-existing comorbid conditions	Chronic obstructive pulmonary disease (COPD) exacerbations, glycemic emergencies, hypertensive emergencies
Malignancy related	Oncologic emergency—tumor lysis syndrome, hyperviscosity, hypercalcemia, airway compromise, disseminated intravascular coagulation (DIC), seizures, and intracranial hypertension
Treatment-related	Chemotherapy-induced toxicities Radiation-induced toxicities Postoperative, after high-risk surgery Postoperative complications such as anastomotic dehiscence, and secondary hemorrhage. Anaphylaxis Cytokine storm Drug-induced coronary spasm or congestive cardiac failure Febrile neutropenia Tumor lysis syndrome (TLS) Differentiation syndrome
Infection related	Neutropenic sepsis Invasive fungal infections Septic shock
Miscellaneous	Transfusion-related circulatory overload Transfusion-related acute lung injury Drug-induced polymyositis

policies practiced for admitting oncology patients into critical care units are as follows [17]:

- Full code—patients are admitted for aggressive life support care anticipating complete recovery and good ICU free survival, for example, newly diagnosed malignancy, cured malignancy, and postoperative patients.
- ICU trial—patients are admitted for aggressive life support with periodic reevaluation, for example, in cases where cure is probable or the therapeutic response to treatment is uncertain. In cases of no improvement after 3–5 days, treatment escalation is withheld.
- Limited ICU Trial—ICU admission for patients with clear advance directives, only for partial life support with no escalation, for example, for procedures as a part of palliative care, not provided in the ward (e.g., noninvasive ventilation).
- Exceptional ICU admission—even in cases that would have been otherwise rejected, ICU admission may be considered at times for the management of acute and reversible causes, for example, dyselectrolytemia, diabetic ketoacidosis and for observation after high-risk interventions.
- Prophylactic admission—for expected tumor lysis syndrome (TLS) or early in course of acute renal failure or in case of anticipated tumor bleeding in high-risk cases.
- Miscellaneous—not fitting in the above criteria, especially when there is a conflict regarding the intention of treatment and treatment goals among intensivist/primary physician/relatives.
- NO admission—the intensivist at times denies admission to patients who are unlikely to benefit from ICU admission, for example, patients with advanced malignancy, who have failed on all possible treatment regimes, and moribund patients.

32.2.1 Trends in Onco-Critical Care

- As the uncertainty surrounding the benefit of critical care in oncology reduced over years, oncologic admissions to critical care units have significantly increased. Current data sug-

gest that oncology patients occupy almost 15–20% of total ICU beds in developed countries and approximately 6% among Indian ICU beds [17, 19, 20]. Over years, there has been a better understanding of disease processes, better preventive strategies, evidence-based management of organ dysfunction, increased use and familiarity with noninvasive modalities for diagnosis and management of acute respiratory failures such as noninvasive ventilation (NIV) and high-flow oxygen by nasal cannula (HFNC), newer antimicrobial agents to combat infections, clear transfusion policies, and early recognition of rare conditions like macrophage activation syndrome and cytokine storm and complications such as drug toxicities [4, 17]. Due to increased familiarity with the common chemotherapeutic agents, the ICU staff are currently capable of administering chemotherapy in patients admitted to the ICU with life-threatening oncologic emergencies such as hyperleukocytosis, TLS, and hemophagocytic lymphohistiocytosis. All these together have reduced the time lag to treatment and has led to a significant reduction in mortality. Currently, ICU survival of oncology patients is at par with any other critically ill patients having comorbidities such as heart failure and liver cirrhosis [21]. More importantly, the patients who survive ICU have been shown to have an excellent quality of life comparable to non-ICU patients [17].

32.2.2 Challenges in Onco-Critical Care

- Cancer patients form a vulnerable group because of their primary disease, chemotherapy/radiotherapy related toxicities and organ dysfunction, immunocompromised status, and in case of cancers of the head-neck region—a physiologically and anatomically challenging airway [1, 7]. At times, they present with oncologic emergencies such as TLS, airway emergencies such as mediastinal masses causing airway compression and airway compromise, obstruction of superior vena cava, metabolic emergencies such as hypercalcemia and hyponatremia, and circulatory complications related to the hyperviscosity states. They are prone to fulminant sepsis due to neutropenic states and otherwise rare complications such as macrophage activation syndrome. Drastic elevations of cytokines like interferon-gamma, interleukin (IL)-10, IL-6 (cytokine storm), and resultant life-threatening complications including capillary leakage, hypotension, and acute respiratory distress are seen in patients receiving chimeric antigen receptor-modified T cells (CART) [22]. Oncological postoperative patients often have a severe inflammatory response due to extensive tissue handling, prolonged surgeries, massive blood loss, and increased blood transfusion requirements. Certain surgeries like pancreaticoduodenectomy and esophageal surgeries are often associated with a stormy ICU course due to surgical complications and medical complications including postoperative respiratory failure [8].

32.3 Critical Care Issues in Oncology

Oncologic emergencies (metabolic or nonmetabolic) are a common cause of ICU admission in oncologic critical care. A brief introduction to the diagnosis and management of these are mentioned below.

32.3.1 Tumor Lysis Syndrome (TLS)

Acute TLS is a serious and life-threatening emergency among patients with aggressive tumors such as Burkitt's lymphoma and leukemias, and some solid tumors [23]. Chemotherapy induces massive cell destruction and release of large amounts of intracellular nucleic acids, phosphorous, and potassium into the circulation. In aggressive and rapidly proliferating tumors, tumor lysis can also occur spontaneously. The nucleic acids are broken down by xanthine oxidase into uric acid, which being water-insoluble,

crystallizes causing acute urate nephropathy, cardiac conduction defects, and gout. Phosphorous binds with calcium, (reducing serum calcium levels dangerously) and form calcium phosphate crystals which in turn can worsen renal failure and urate nephropathy. Dangerously high levels of serum potassium and low calcium together can lead to cardiac conduction defects and death. The kidneys try to handle elevated phosphorous and potassium levels by increased elimination. In cases of acute renal failure, or in cases where the electrolyte levels rise above the kidney's capacity to excrete them, life-threatening arrhythmias can occur. Early identification and adequate hydration (200 ml/kg/day or 2–3 L/m^2—targeting a urine output of 100 ml/m^2) in high-risk cases reduces the severity of tumor lysis. Other medical management includes reduction of uric acid production by allopurinol (xanthine oxidase inhibitors) or urate oxidase inhibitors like rasburicase administration (if not contraindicated) along with potassium-binding resins and phosphorous-binding resins (Sevelamer). Renal replacement therapy might be required in cases of signs of fluid overload or severe life-threatening hyperkalemia. A calcium phosphorous ratio of more than 60 in the setting of tumor lysis syndrome along with worsening renal failure and oliguria also predicts the possible requirement for renal replacement therapy [24–26]. Management of tumor lysis syndrome is outlined in Fig. 32.1.

32.3.2 Hypercalcemia

Approximately 10–20% of cancer patients develop hypercalcemia sometime in course of their malignancy. Hypercalcemia is commonly associated with multiple myeloma, cancers of lung, breast, head and neck region, T-cell lymphomas, renal carcinoma, etc. The clinical presentation is nonspecific with presenting symptoms like confusion, nausea, constipation, polyuria, lethargy, which if uncorrected can progress to coma and death. An increased circulating parathyroid hormone-related peptide (PTHrP), parathyroid hormone (PTH) over secretion, vitamin D overproduction by lymphoma cells, or direct osteolytic destruction of bone by tumor are the major causes for hypercalcemia. Management includes aggressive rehydration, calcitonin for the initial period, followed by intravenous bisphosphonates. Steroids can be tried if the etiology is suspected to be of the granulomatous

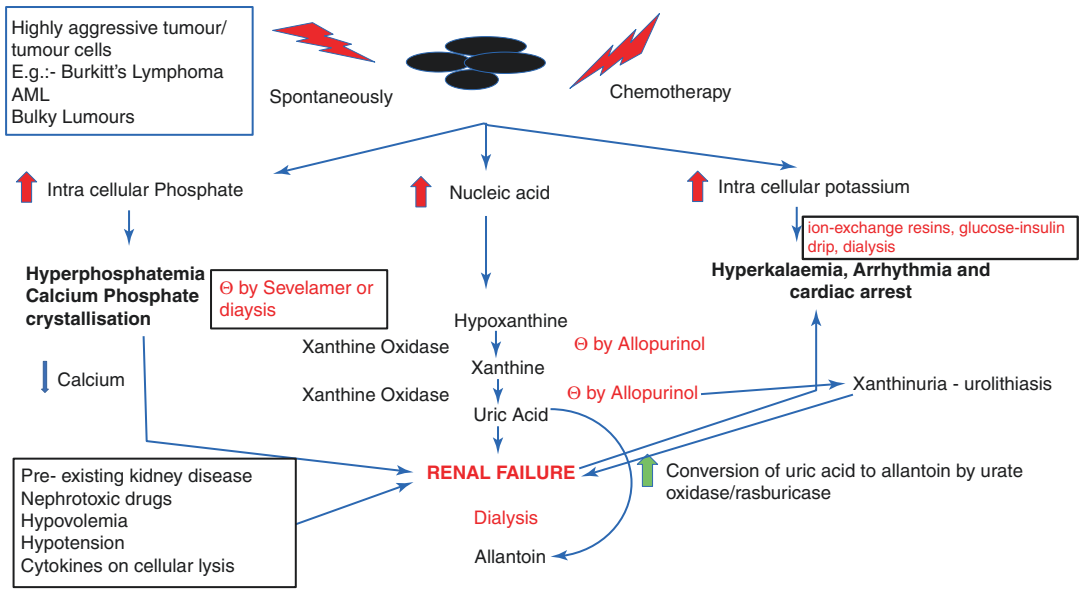

Fig. 32.1 Management of tumor lysis syndrome

origin or if associated with lymphomas. As with tumor lysis, dialysis may be required for metabolic correction if hypercalcemia is resistant to ongoing medical treatment, presence of comorbidities that contraindicate aggressive hydration, or in cases of acute renal failure [23, 24].

32.3.3 Hyponatremia

Hyponatremia is a common occurrence in malignancy and can be either directly related to the disease or therapy. The pathophysiology may be related to the underlying syndrome of inadequate ADH secretion (SIADH) or hypovolemia. At times patients present with acute onset of hyponatremia (of duration less than 48 h) commonly seen among patients with psychogenic polydipsia, after chemotherapy with intravenous (iv) cyclophosphamide, in postoperative patients (due to intraoperative or postoperative administration of hypotonic fluids) or following therapy with laxatives for colonoscopy preparation [27]. The threshold of 48 h is because the brain requires 48 h to adapt to a hypotonic state of hyponatremia by resetting the osmotic equilibrium. After 48 h, the brain is vulnerable to the adverse effects of the acute rise in serum sodium, such as pontine and extra pontine osmotic demyelination syndrome. Cancer patients are at increased risk of demyelination because of associated malnutrition and hypokalemia. Common causes of SIADH in cancer patients include drugs, cancer per se, infections, and other associated causes (Table 32.2) [27, 28]. In ICU, the evaluation of hyponatremia includes acquiring necessary information from histories such as symptoms and duration, clinical assessment of volume status, and laboratory evaluation such as urine osmolality and urine spot sodium, serum osmolality (to distinguish between true and pseudo hyponatremia), and fractional excretion of sodium and urea. A practical algorithm toward the approach to hyponatremia can be adapted from reference [27]. As cerebral edema is a potential killer, for patients presenting with symptoms of raised cerebral edema such as headache, vomiting, confusion, seizures, or altered level of consciousness—irrespective of duration and degree of hyponatremia, treatment should be initiated with 2–4 ml/kg of 3% saline as a bolus over 20 min with repeated dosing, if the patient is still symptomatic and acute rise is less than 10 mmol/day [27].

Table 32.2 Common etiologies of SIADH

Drugs	Cyclophosphamide, cisplatin, vinca alkaloids, methotrexate, cyclophosphamide Valproic acid, carbamazepine, and oxcarbazepine Morphine, NSAIDs Proton pump inhibitors
Infections	Infections like TB and pneumonia, meningitis, encephalitis
Primary malignancy itself	Small-cell carcinoma of the lung, head and neck region, upper gi malignancies (stomach, pancreas, and duodenum), endometrium, bladder, and prostate
Miscellaneous	Pain, nausea, cerebrovascular accidents, general anesthesia, positive pressure mechanical ventilation

32.3.4 Acute Respiratory Failure

Acute respiratory failure (ARF) is the leading cause of ICU admission among patients with malignancy [29]. ARF has an incidence of 5–50% in patients with hematologic and solid malignancies and an increased incidence of 42% up to 88% among hematopoietic stem cell transplant recipients [30, 31]. The etiological diagnosis of ARF are varied and include infections, pulmonary edema, treatment-induced lung injury, diffuse alveolar hemorrhage [DAH]), pulmonary embolism, airway obstruction secondary to disease progression. In postoperative patients, type III respiratory failure may also occur [32].

Pulmonary infections are the commonest cause of ARF in patients with cancer. The majority of the infections are caused by common bacterial agents [33]. Opportunistic infections of the lung such as invasive pulmonary aspergillosis, *Pneumocystis jirovecii* pneumonia, mucormycosis, cytomegalovirus, and other respiratory viral infection are also important etiologies for respi-

Table 32.3 Etiology of ARDS among cancer patients

Pulmonary infection	Secondary causes	Disease/treatment-related	Miscellaneous
Gram-negative and gram-positive bacterial infections Fungal infections including invasive pulmonary aspergillosis *Pneumocystis jirovecii* Viral diseases like influenza Tuberculosis	Secondary ARDS (extrapulmonary ARDS) Secondary to sepsis	Drug-induced and radiation-induced Transfusion-associated acute lung injury (TRALI) Autoimmune Lymphangitis carcinomatosis Pulmonary alveolar proteinosis Bronchiolitis obliterans and organizing pneumonia Hemophagocytic Lymphohistiocytosis Pulmonary leukostasis/leukemic infiltration Postengraftment syndrome	Unclear etiology

ratory failure. Prolonged neutropenia, administration of corticosteroids, broad-spectrum antibiotics, and hematologic malignancies are risk factors for invasive fungal infections. Infections are also the major cause of acute respiratory distress syndrome (ARDS) in these patients although secondary ARDS can also occur following septic shock. The common etiologies for ARDS among cancer patients are shown in Table 32.3.

It is often challenging to come to an etiological diagnosis and the inability to identify an etiology is an independent predictor of mortality [34]. Recently, the practice has changed from invasive investigations like bronchoscopy, bronchoalveolar lavage (BAL), and surgical lung biopsy to noninvasive investigations like high-resolution computed tomography (CT), biomarkers, and molecular tests [35]. The majority of these patients will be at risk of invasive fungal infection due to prolonged neutropenia and multiple antibiotics. Signs such as lobar pneumonia, bronchopneumonia, cavitating pneumonia, feeding vessels, halo sign, and ground glassing with the tree in bud appearance on CT scans aid in supporting the etiological diagnosis of bacterial pneumonia, atypical pneumonia, or fungal pneumonia, tuberculosis, etc. (Table 32.4). None of these radiologic signs (air bronchogram, halo sign, ground glassing tree in bud appearance) are specific or sensitive and need to be correlated with microbiological investigations such as galactomannan and polymerase chain reaction (PCR) of a directed or nondirected BAL [36]. Galactomannan detected in different body fluids with a cut-off of 0.5 is sensitive and specific enough to diagnose invasive pulmonary aspergillosis. As nonneutropenic patients' clear galacto-

Table 32.4 Common radiologic patterns in ARF on CT scan

Radiological signs	Probable etiological diagnosis
Lobar consolidation with air bronchogram	Typical bacterial pneumonia, viral pneumonia
Cavitation	Staphylococcus, Klebsiella, tuberculosis, cavitating malignancy, etc.
Patchy consolidation	Focal atelectasis, organizing pneumonia, atypical pneumonia
Ground glass opacities (GGO)	Pulmonary edema, vasculitis, interstitial lung disease, atypical bacterial pneumonia, viral pneumonia
Miliary pattern	Tuberculosis
Air fluid level	Lung abscess, hydropneumothorax
Air crescent sign	Aspergilloma/fungal ball
Halo sign	Aspergillosis
Reverse halo	Aspergillosis, mucormycosis, cryptogenic organizing pneumonia
Crazy paving	Pneumocystis pneumonia, viral pneumonia
Feeding vessel sign	Septic embolism

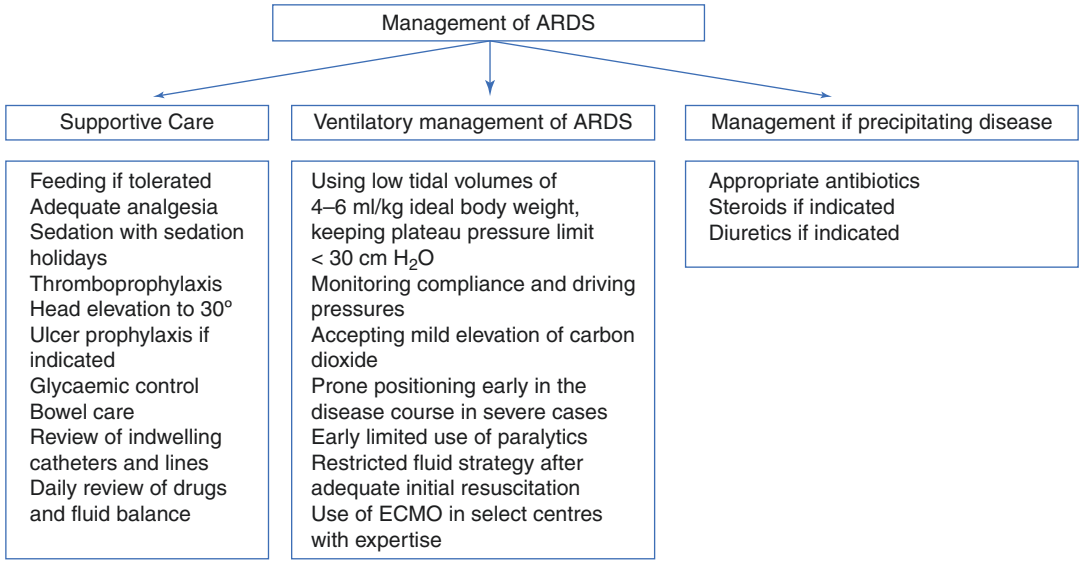

Fig. 32.2 General principles of ARDS management

mannan rapidly from their body, this test cannot be recommended in them [37].

32.3.5 Management of Acute respiratory distress syndrome (ARDS) in ICU

In cancer patients with acute respiratory failure, increased mortality has been observed to be associated with oxygen requirement and the risk exponentially increases if ventilatory support is required. Historically, ARDS among oncology patients had a dismal prognosis and high mortality. With an evolving understanding of disease pathophysiology and the current practice of lung-protective mechanical ventilation strategies, there has been a remarkable drop in the in-hospital mortality of cancer patients with ARDS. With a multimodality approach, including low tidal volumes, limiting plateau pressure to less than 30 cm of water, prone positioning in severe ARDS early in the disease course for prolonged periods, permissive hypercapnia, early but limited use of muscle relaxants, the mortality of ARDS has reduced from 89% to 59%, 63%, and 68.5%, respectively, in mild, moderate, and severe ARDS groups [33, 38]. The general principles of ARDS management are outlined in Fig. 32.2.

32.3.5.1 Role of Noninvasive Ventilation (NIV) in ARDS Management

As mentioned earlier, the initial treatment outcome for ARDS patients requiring intubation and mechanical ventilation was very high and up to the ranges of 80% or more mortality [39]. It was then hypothesized that if respiratory support was provided without intubation, the mortality might fall. Initial small studies hinted at the same [39–41], and NIV was advocated as an initial option to manage ARDS in immunosuppressed patients [42]. This was debated as further trials failed to replicate similar beneficial findings [43]. A multicentric trial from France failed to demonstrate any difference in mortality among early NIV versus oxygen therapy [44]. Similarly, the recently concluded EFRAIM study also could not find any association between NIV and mortality benefits [45]. A gradual but significant reduction in the ARDS mortality over years due to a general improvement in critical care and better ventilation strategies together with the potential harms of high tidal volume and swings in pleural pres-

sure in NIV are the reasons postulated for the discrepant trials [17]. The initial enthusiasm for NIV against intubation has currently plateaued, and current literature suggests overall NIV failure rates of 70%, particularly in severely ill patients [34]. It is currently clear that early NIV does not improve mortality rates nor does it fare better than high-flow oxygen therapy. As NIV failure is a proven risk factor for increased mortality [33], till further studies are available, NIV should be judiciously used in these patients and preferably avoided among patients with moderate to severe ARDS [17, 45].

32.3.5.2 Role of High-Flow Oxygen Therapy in ARDS Management

High-flow nasal cannula (HFNC) delivers 100% humidified oxygen with flow rates up to 60 l/min. These high flows generate a flow-dependent positive end-expiratory pressure (up to 7 cm of water), maintain alveolar recruitment, improve oxygenation, and reduce the work of breathing [46]. Hence, it seems probable that HFNC might significantly reduce intubation rate and mortality in patients with hypoxemic respiratory failure. The FLORALI trial showed a trend toward reduced 90-day mortality in hypoxemic respiratory failure patients (which also included immunosuppressed patients) treated with HFNC compared to those treated by NIV [47]. A retrospective study among cancer patients also suggested a survival benefit with HFNC compared to NIV [48]. Similar results (reduced intubation rates and mortality rates) were also seen in an observational cohort study with HFNC faring better than NIV [49]. A recent meta-analysis of trials looking into HFNC in immunocompromised patients suggests that the use of HFNC improves the outcomes of acute respiratory failure in immunocompromised patients significantly. However, good quality studies that are adequately powered to confirm these benefits are still lacking [50].

32.3.6 Sepsis

Overwhelming infection and sepsis can occur in the setting of oncology as patients are immunosuppressed due to the disease, treatment, and following myeloablative therapy for bone marrow transplant. Mortality of sepsis is associated with the underlying organ dysfunction rather than the characteristics of malignancy such as neutropenia or disease progression [51]. The pathophysiology of sepsis and septic shock remains the same to noncancer patients, and no clinically significant differences in the macrocirculation or the microcirculation have been demonstrated [52]. Oncology patients are usually neutropenic (absolute count of polymorphonuclear neutrophils (PMNs) less than 500/mm^3) due to the disease involvement or treatment complication (chemotherapy and radiotherapy). Profound neutropenia (absolute count of PMN less than 100) and duration of neutropenia for more than 7 days are risk factors for severe infections. These patients seldom mount an immune response to infections, and hence, there is a delay in identifying infections in these patients. Febrile neutropenia (FN) is defined as a single reading of oral temperature more than 38.3 °C (101 °F) or an oral temperature recording of more than 38.1 °C (100.4 °F) sustained over a 1-h period in patients with an absolute neutrophil count less than 500 cells/mm^3 or in whom absolute neutrophil count is expected to decrease to less than 500 cells/mm^3 during the next 48 h [53, 54]. Patients usually present with pneumonia, gastroenteritis, urinary tract, or primary bacteremia. Sepsis is a medical emergency similar to polytrauma, acute myocardial infarction, and stroke. The Surviving Sepsis Campaign stresses early identification and management of sepsis with appropriate measures such as initial hydration (30 ml/kg crystalloids), hemodynamic monitoring, and use of vasopressors and antibiotics. They suggest a 1-h bundle approach that incorporates initial resuscitation with ongoing evaluation [55]. With early identification and improved care, the mortality rate of sepsis has come down and is currently reported as low as 40% in cancer patients [55, 56]. Currently, sepsis is managed in lines with the management protocols of patients without malignancy. Adjuvant G-CSF in neutropenic sepsis, and rather it may worsen the respiratory status due to pulmonary infiltration by leucocytes [57].

The dilemma in the management of this emergency is that all these patients will be either hospitalized or having frequent contact with the hospital and already might have received multiple antibiotics. Hence, these patients are at increased risk for severe infections by multidrug-resistant organisms. The treating intensivist will have to choose the initial empirical antibiotic therapy based on the treatment history, and local antibiogram, and later deescalate according to culture reports and treatment response. Consideration should be given to multidrug-resistant (MDR) organisms, rare opportunistic organisms, and fungal organisms while selecting the initial empirical treatment regime. Patients who present with organ dysfunction and septic shock should be treated with a broad-spectrum agent such as carbapenem or even polymyxins like colistin and polymyxin B, depending on the local antibiogram and the presence of shock and organ failure. Multidrug combination therapy with a third-generation or fourth-generation cephalosporin and an aminoglycoside [53] or meropenem and polymyxin targeting most aerobic gram-negative bacteria may also be used. The empiric gram-positive cover needs to be added if the local incidence of MRSA is high, if patients present with hemodynamic instability, or there are infiltrates on chest X-ray suggestive of pneumonia [54]. Patients in shock or those who fail to improve should be treated with additional antifungal agents such as echinocandins or amphotericin B [54, 58]. Patient characteristics such as neutropenia, diabetes mellitus, chronic renal failure, invasive vascular devices, prolonged broad-spectrum antibiotics, multisite fungal infection, or colonization are considered high risk for invasive candidal infection. If the risk of Candida sepsis is high, empiric antifungal therapy may be initiated on admission itself [59].

32.3.7 Airway Emergencies

Airway obstruction from either local compression by mediastinal malignancies can cause mechanical respiratory compromise requiring ventilatory assistance. Patients present with stridor, dyspnea, hemoptysis, and cough, and some may have features of superior vena cava syndrome. An emergency CT scan of the thorax may help to differentiate among various causes of acute breathlessness and gives an idea of anticipated complications in securing the airway. Bronchoscopy (rigid or flexible depending upon expertise) can also be used as a diagnostic and curative tool. The treatment requires expedited management of the local cause and includes radiation therapy if the tumor is radiation sensitive or chemotherapy for highly chemosensitive malignancies like lymphomas, small cell lung cancers, and germ cell tumors [60]. Thymic tumors can cause myasthenia, as well as exert direct tracheal compression. In such cases, excision of the mass can alleviate the respiratory compromise and cure myasthenia in a significant percentage of patients. These groups of patients require constant vigil of the airway and urgent intubation in case of respiratory failure.

32.3.8 Acute Abdomen

Cardiac dysfunction can result from the mechanical effect of the malignancy on the heart, pericardium, and great vessels. The chemotherapeutic agents used for managing cancer can cause cardiomyopathy resulting in an impaired systolic and diastolic function of the heart. Commonly implicated agents are anthracyclines like doxorubicin, and newer chemotherapeutic agents like trastuzumab [61]. Patients present with arrhythmias or electrocardiography (ECG) changes such as QTc prolongation, breathlessness, or in frank cardiogenic shock. Cardiac failure is managed in similar lines of cardiac failure in noncancer patients with noninvasive ventilation, diuretics, vasodilators, and inotropes. Preemptive treatment with angiotensin-converting enzyme (ACE) inhibitors alone, or in combination with beta-blockers and dexrazoxane has been advocated in preventing cardiac failure among high-risk patients [62].

Radiation-associated cardiotoxicity is usually seen in young patients and presents later in life. The toxicities described include coronary artery disease, regurgitant or stenotic valvular pathologies, dilated

cardiomyopathy, conduction defects, and heart failure with preserved ejection fraction. Pericarditis can occur either acutely or as late as 6 months to 1 year after radiotherapy. Constrictive pericarditis presents with features of heart failure with a calcified noncompliant pericardium. These patients will require pericardiectomy although diuretics may provide temporary symptom relief [61].

Right heart failure and pulmonary hypertension (PH) can be associated with chemotherapeutic agents such as dasatinib or following pneumonectomy. Management guidelines for pulmonary hypertension have been published and treatment includes avoiding hypoxia, aggressive management of infections, diuretics, calcium channel blockers, anticoagulants, and pulmonary artery vasodilators [63].

Malignant pericardial effusion and cardiac tamponade due to massive pericardial effusion occur due to malignancies of the breast, lung, or direct involvement from melanoma or leukemia. Patients present with severe dyspnea and orthopnea and dry cough. Bedside echocardiography will reveal the diastolic collapse of cardiac chambers. Pericardiocentesis or pigtail insertion under image guidance may be needed for symptom relief [23, 60].

32.3.9 Cardiac Failure and Cardiac Tamponade

Abdominal malignancies can produce obstructive symptoms depending upon their location. Bowel involvement can lead to subacute intestinal obstruction, intestinal obstruction, bowel perforation, and can present as a surgical emergency. Local involvement of the gall bladder or biliary tract by the tumor can cause biliary obstruction, cholangitis, and jaundice. Tumor infiltration can cause massive bleeding and present as hemorrhagic shock. Compression of the ureters or bladder can cause hydronephrosis and postrenal kidney injury. The management will depend upon the cause and at times may require emergency laparotomy. Selective angiographic embolization can control tumor bleed, whereas local drainage by stenting such as biliary stenting and ureteric stenting can be done by the interventional radiologist for symptom relief and management. Hence, a good liaison between the surgical team, diagnostic and interventional radiology, and intensivist is required to manage these patients [64, 65].

32.3.10 Central Nervous System (CNS) Emergencies

Primary malignancies of the CNS can present with altered sensorium, seizures, or features of raised intracranial pressure (ICP). Unless intervened urgently, trans-tentorial herniation and death can ensue. The management in these cases remains surgical decompression. However, osmotherapy with mannitol or hypertonic saline, corticosteroids, and good ICU care, including sedation, paralysis, maintaining normothermia, maintaining normoxia, normoglycemia, eucarbia, may help as a temporary measure to reduce raised intracranial pressure. Epidural or bony metastasis from underlying lung cancer, breast cancer, and multiple myeloma, lymphoma, prostate cancer, etc. can cause cord compression and may present with features of paraplegia. Patients usually present with symptoms such as pain, motor weakness, sensory symptoms, bowel, and bladder involvement, early suspicion, diagnosis, and management are pivotal for recovery. Management includes immediate administration of glucocorticoids, surgery, radiotherapy, and systemic therapy in patients with chemosensitive tumors [66].

32.3.11 Adrenal Crisis or Adrenal Insufficiency

Adrenal insufficiency due to metastases or infiltration of bilateral adrenals with malignancy, surgical excision of both glands, or adrenal hemorrhage in severe sepsis, can cause adrenal insufficiency in patients with malignancy. At least 90% of functioning adrenal tissue must be lost for symptoms to manifest. Patients usually present with vague features like nausea vomiting, diarrhea, vague abdominal or flank pain, confusion, and vasopressor resistant hypotension. Hyponatremia, hyperkalemia, and mild acidosis may be seen in

biochemical analysis. Cancers of lung, breast, kidney, stomach, and pancreas are the common types to metastasize adrenals. A positive cosyntropin stimulation test suggests the diagnosis, and these patients need to be supplemented with daily physiologic doses of glucocorticoids [67].

32.4 Postoperative Care in Oncology

The back-up of critical care in postoperative care resulted in the undertaking of advanced and more aggressive procedures like tracheal resection and heated intraperitoneal chemotherapy (HIPEC) that have a positive influence on survival. Oncologic surgeries are associated with extensive tissue dissection, fluid shifts, and third space loss, cardiac arrhythmias, electrolyte imbalance, impaired glucose control, hypothermia, etc. Postoperatively, they are prone to a higher risk of surgery-related complications such as postoperative bleeding, respiratory failure, malnutrition, and venous thrombosis, which need to be addressed urgently. Apart from these, all patients will require routine post-operative care such as care till complete recovery from anesthesia, optimizing pain medications, managing postoperative nausea, vomiting, and other complications such as shivering [7, 68].

32.5 Transfusion Practices in Onco-Critical Care

Oncology patients are excluded from the majority of the blood transfusion trials, and hence, any evidence in these subsets of patients is patchy. In the general population, a restrictive strategy of transfusion for red blood cells is followed, targeting a hemoglobin level above 7 g/dl. This practice has been proved to be safe in a sicker group of patients with sepsis. There have been only two trials in cancer patients—TRISOP (surgical patients) and TRICOP (solid tumors with septic shock). These two trials seem to differ from the general practice of restrictive strategies in favoring a liberal transfusion strategy over a restrictive strategy and point toward the need for further research in this field. However, red blood cells should be transfused with caution in patients with hyperviscosity syndromes—hyperleukocytosis, multiple myeloma, etc. and a restrictive approach might be beneficial in these patients [69].

Cancer patients in ICU will be having a reduced platelet count from underlying malignancy, sepsis, chemotherapy or irradiation, immune destruction as in ITP, antibody-mediated as in heparin-induced thrombocytopenia, etc. Evaluation of the etiology for thrombocytopenia should be considered for platelet count less than 100,000/cc. The evidence regarding platelet transfusion is also limited, and transfusion is currently advocated only in cases of active bleeding or prophylactic when the platelet falls below a threshold of 10×10^9/l or 20×10^9/l, if the patient is febrile [70].

32.6 Chemotherapy in ICU

Administration of chemotherapeutic agents in the ICU is indicated to treat or prevent life-threatening malignancy-related emergencies such as hyperleukocytosis, hemophagocytic lymphohistiocytosis (HLH), and tumor lysis syndrome. Over the years, there has been more experience in administering chemotherapy in the ICU, and this has led to a decrease in the short-term and long-term mortality rates. Caution must be exerted while calculating the required doses, accounting for organ dysfunction, altered pharmacokinetics, and pharmacodynamics of critically ill patients and seeking help from the oncology team will be beneficial. The presence or presumed presence of infection need not hinder chemotherapy in ICU in case of life-threatening emergencies. The patient identity and the chemotherapeutic schedule should be confirmed, cross-checked, and documented and informed consent regarding the adverse effects of the same should be taken before the administration of chemotherapy. Care must be taken while administering these extremely toxic drugs and the recommendations regarding dilution, volume, infusion rate, etc. should be followed. In the case

of drug reactions or drug toxicities, or drug extravasations, the drug infusion should be stopped immediately and help from onco-hematology should be sought [71].

32.7 Infection Control in ICU

Cancer patients are at high risk for nosocomial infections, and the rates can be as high as 40% [72]. Hospital-acquired and ICU-acquired infections escalate the treatment cost and also increases morbidity, mortality significantly. The common nosocomial infections are ventilator/hospital-acquired pneumonia, skin and soft tissue infections, central-line-related bloodstream infections, and catheter-associated urinary tract infections. Because of the huge implication of these infections, a systematic approach to reducing the effects is required. Simple measures like maintaining hand hygiene have been proved to be effective in reducing infection rates in hospitals. All hospitals now adhere to the "five moments of hand washing" as suggested by the World Health Organization (WHO)—that is, before and after touching a patient, before any sterile procedure, after contact with fomites in patient surroundings, and after any high-risk procedures with body fluid exposure [73]. The hospital-acquired infection rates are considered benchmarks of poor compliance of healthcare staff with the handwashing guidelines. Apart from hand hygiene, many bundles (a group of interventions that performed together changes the outcome efficiently) have been suggested to reduce HAI. The bundles for infection control have been summarized in Table 32.5 [74].

Table 32.5 Common bundles in ICU for infection control

Ventilator-associated pneumonia (VAP) bundle	Head end elevation of the bed up to 30° Daily interruption of sedation and spontaneous breathing trials Aspiration of subglottic secretions Peptic ulcer prophylaxis in high-risk patients Deep vein thrombosis prophylaxis
Central line related blood stream infection (CRBSI) bundle	Maintaining good hand hygiene practices Strict aseptic precautions for line insertion Use of chlorhexidine for skin antisepsis Preference for subclavian and jugular sites than femoral sites Daily assessment of lines and prompt removal of unnecessary lines
Catheter associated urinary tract infection (CAUTI) bundle	Avoid unnecessary urinary catheterizations Catheterize in aseptic precautions Daily care of urinary catheter and remove if not required

32.8 Nutrition in Onco-Critical Care

Malnutrition is a common problem among critically ill oncology patients and is aggravated by infections, inflammation, stress, etc. The previous nutritional status of the patient is also an important factor affecting malnutrition. Most of these patients will be malnourished due to preexisting nausea, vomiting, and cachexia of malignancy. Malnutrition results in increased morbidity and mortality in all patients, and hence, nutritional support should be initiated early aiming to minimize the effects of starvation, support the immune system, prevent nutritional deficiencies, and facilitate wound healing. Screening tools like Nutritional Risk Screening 2002 (NRS 2002), the malnutrition universal screening tool (MUST) mini nutritional assessment (MNA), and the malnutrition screening tool (MST) are available to rapidly screen patients at risk for malnutrition. Clinical parameters that hinder nutrition like disease site, anorexia, asthenia, vomiting, dysgeusia, pain, depression should be actively searched for. A significant weight loss (>10% for 6 months) is the most reliable indicator of nutritional deficit. Albumin and prealbumin can be altered by infections, liver diseases, renal dysfunction, dehydration, anasarca, etc., and this limitation must be kept in mind. The European Society for Clinical Nutrition and Metabolism (ESPEN) guidelines recommend dual X-ray absorptiometry (DEXA) or bioimpedance analysis (BIA) to assess muscle

Table 32.6 Indications of total parenteral nutrition in ICU

Contraindication to enteral feeding	Chyle leak Intestinal obstruction
Malfunctioning gut	High-output enterocutaneous fistulas Paralytic ileus Massive resection of bowel Radiation enteritis Not attaining nutritional goals even after 2 weeks
Inadequate enteral feeding	Patients at high nutritional risk with anticipated delay in attaining nutritional gals by 7 days

mass and fat reserves, along with performance scales such as the Eastern Cooperative Oncology Group (ECOG), or Karnofsky and biomarkers such as serum C-reactive protein (CRP) and albumin for nutritional assessment in high-risk patients. Enteral feeding is safe and effective and if tolerated should be initiated early in the course of ICU stay. There has been no evidence for immune nutrients in cancer patients though it seems attractive and physiological. Those who have a high nutritional risk score and contraindications for enteral feeding may be considered for early parenteral nutrition. Patients with anorexia but a functioning intestinal tract have not been shown to benefit from parenteral nutrition, and, therefore, priority should always be given to the enteral route [75]. Total parenteral nutrition is indicated only in a select population in the ICU (Table 32.6).

32.9 ICU Outcomes of Cancer Patients

Patients with solid tumors seldom require ICU admission for medical reasons such as febrile neutropenia, septic shock, invasive fungal infection, acute respiratory failure, or other organ dysfunctions. The majority of these patients will be admitted to the critical care unit postoperatively. Excluding patients admitted for routine postoperative care, patients with solid tumors have almost double mortality rates as compared to patients without cancer (41% vs 21%) [76].

Hematological patients on the contrary are usually admitted to critical care units for life-threatening medical conditions such as oncologic emergencies, infections, or organ dysfunction. They generally tend to have higher disease severity scores [Simplified Acute Physiology Score (SAPS II)] or sequential organ failure assessment score (SOFA score) and a higher mortality rate (50–60%) [76].

Bone marrow transplant (BMT) recipient patients remain a separate subset with high ICU and in-hospital mortality, even though the mortality rates are decreasing. BMT patients require ICU admission for medical complications like acute respiratory failure, sepsis, cardiac dysfunction, neurologic disorders, and bleeding diathesis. BMT patients requiring mechanical ventilation still have an ICU mortality rate of 80% that further worsens with worsening organ dysfunction [16]. Various factors affect the prognosis of critically ill patients admitted to an ICU (Table 32.7).

32.10 Palliative Care in ICU

Palliative care is defined as a holistic approach to improving the quality of life of patients and their families by early identification, meticulous assessment, and addressing unmet needs such as pain and other physical, psychosocial, and spiritual problems [79]. The key domains include (1) symptom management; (2) empathetic and realistic communication about disease, possible treatment, and outcomes; and (3) support for both patient and family throughout illness. Palliative care is an integral component of multidisciplinary care and should be provided to all. The initiation of palliative care is associated with better control of symptoms, better utilization of hospice resources including ICU stay, increased satisfaction for patient and family, and reduced moral stress on the physician, thus minimizing burnout. The barriers to palliative care can be minimized by effective and realistic communication, discussing advance directives (if present), with care to avoid confusing words such as withdrawal of care and use simple realistic terms like

Table 32.7 Prognostic factors for critically ill oncology patients [76–78]

Negative prognosis	Positive prognosis	Neutral
Extreme ages Respiratory failure requiring mechanical ventilation Delay of >2 h in starting appropriate empirical antibiotics Multiple organ dysfunction score > 2 organ involvement Higher apache/sofa scores Invasive aspergillosis Poor response of cancer to chemotherapy Poor performance score before ICU admission—Karnofsky score <70 or higher Eastern Cooperative Oncology Group (ECOG) scale 3–4	Indication for ICU admission being primary postoperative care Disease in remission Good performance status before hospital admission Acute onset of critical illness (< than 7 days) Absence of fungal infection Absence of comorbidities Reversible cause for ICU admission	Type of tumor (solid vs hematological) Neutropenia Metastatic nature of the disease Prior ICU admission

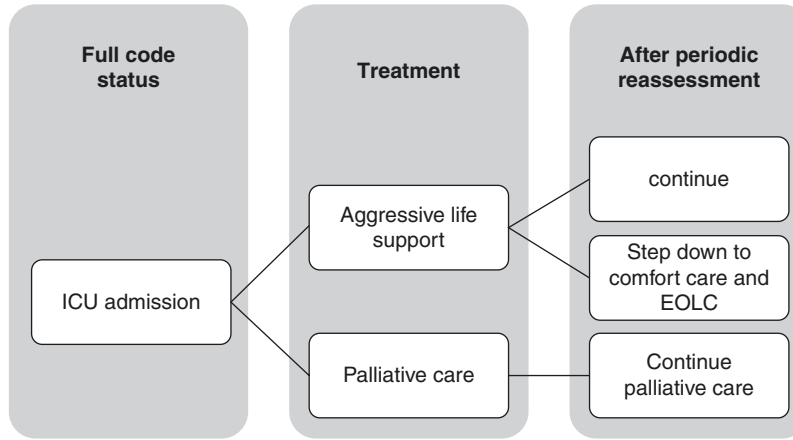

Fig. 32.3 Schematic representation of patient care in ICU

withdrawal of life-sustaining treatments [80–82]. A schematic representation of ideal patient care in ICU is represented in Fig. 32.3.

32.11 End-of-Life Care (EOLC) in ICU

Ideally, only those patients who have a reasonable chance of either cure or palliation from their disease or symptoms should be admitted to a critical care unit. However, many times patients with advanced disease or those with advanced directives will be admitted to the ICU for a time-limited full-code trial. Although seemingly straightforward, the transition from full-code status to EOLC is often vague, delayed, and an area of conflict. This creates a situation of dilemma, conflict of interests, and the increased patient suffering from simultaneous wastage of resources. At a stage of treatment futility or end of life, intensive care to the patient should mean comfort care, avoidance of inappropriate aggressive interventions clearly understanding that aggressive life-supporting interventions increase rather than alleviating the sufferings of the patient. The treatment plan of all critically ill patients should be revised frequently and monitored for futility. If futility is observed, it should be conveyed to the primary team and relatives. Open empathetic communication with relatives and the primary team is required to voice opinions while avoiding conflict. EOLC discussions require time and multiple sessions of discussions. Each session must be documented properly to maintain transparency. Once EOLC is decided, the site of care should be reviewed, with preference to patient comfort. Adequate space for the patient and relatives, adequate medications, adequate staffing needs to be

ensured and the patient should not be neglected at any point in time. Unnecessary monitoring may be avoided, and close relatives may be permitted to remain by the bedside, as per their wishes. All treatment orders should be reviewed, with unnecessary medications being avoided but retaining medications for symptom control. There should be regular assessment regarding the adequacy of treatment for symptom control. Spiritual care should also be taken care, and bereavement support to the family members should be offered to cope with their issues [83, 84].

32.12 Integrated Intensive Care Management of Onco-Critical Care

Intensive care for critically ill cancer patients requires an integrative approach from the oncologist, intensivist, primary physician (in case of surgical specialty, or nononcological specialty). Whenever a patient arrives at the hospital for the initial visit, the nature of the disease and possible treatment options should be realistically and empathetically explained to the patient and relatives. This allows them to be realistic and prepare for the disease and treatment complications. On follow-up, response to treatment must be evaluated and any change in the treatment plan should be discussed and documented. Addressing the patients' unmet needs like symptom management and palliative care should be involved at this stage, if not involved earlier.

When there are signs of organ dysfunction or sepsis, broad-spectrum antibiotics need to be administered while preparing for a discussion with intensive care. As none of the current tools can accurately predict patients who may benefit from intensive care, all patients willing to be shifted to ICU, and those without advanced directives may be shifted to the ICU. All patients with advanced disease and in whom no treatment can be offered for control of the primary disease may be refused ICU admission. During ICU stay, there should be daily interaction among the intensivist and oncologist regarding response to therapy and prognosis. All patients admitted to ICU should receive full-code treatment, similar to noncancer patients for the initial 3–5 days, unless specified. Patients identified for end-of-life care should be initiated for the same after detailed discussion and appropriate documentation among caregivers and relatives. Patients discharged from ICU should be followed up by the intensivist and screened for postintensive care syndrome. Those suffering from depression and other chronic illnesses post-ICU stay must be identified, and rehabilitation must be offered [8, 17, 76]. Figure 32.4 summarizes a flowchart of integrating care from an initial hospital visit to post-ICU discharge.

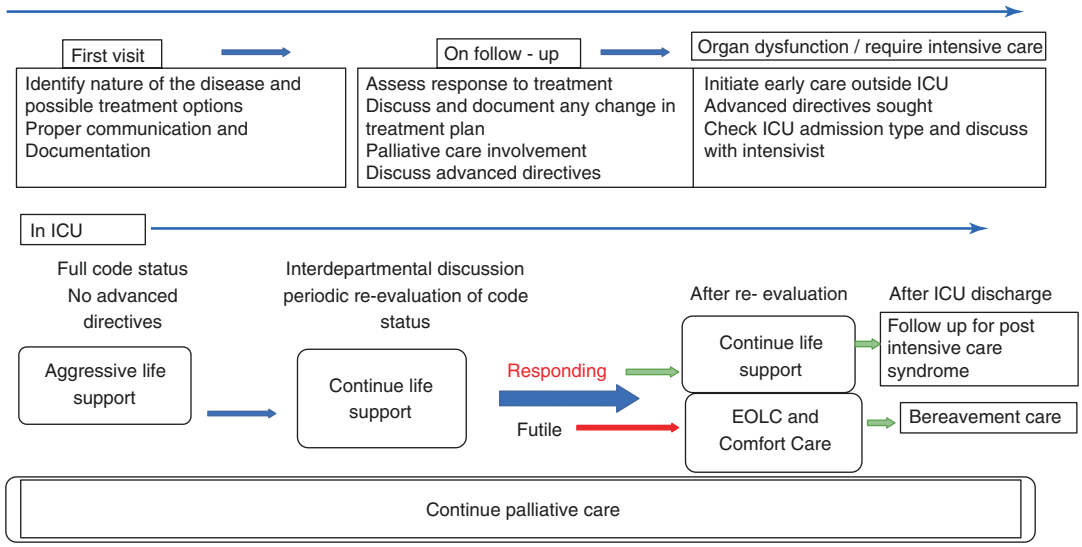

Fig. 32.4 Integrating various departmental services in oncology critical care

32.13 Summary

Intensive care in oncology has evolved over decades and is currently a rewarding profession. Properly selected patients admitted to the ICU have survival rates and quality of life identical to their noncancer counterparts. Early identification of organ dysfunction, potent antimicrobial therapies, and noninvasive diagnostic strategies for organ dysfunction and appropriate management are some of the factors responsible for the reduction in mortality rates. We need to develop a score that predicts benefits for early ICU admission in these subsets of critically ill patients. The strategies used to avoid intubation (like NIV and HFNC) need further evaluation before they are accepted as alternatives to mechanical ventilation. End-of-life care and palliative care are also integral parts of intensive care and should be offered to all eligible patients. For the better outcome of these patients, a multidisciplinary team including intensivist, oncologist, and palliative care specialist is essential.

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