Intensive care in thoracic oncology

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ABSTRACT The admission of lung cancer patients to intensive care is related to postprocedural/postoperative care and medical complications due to cancer or its treatment, but is also related to acute organ failure not directly related to cancer.

Despite careful preoperative risk management and the use of modern surgical and anaesthetic techniques, thoracic surgery remains associated with high morbidity, related to the extent of resection and specific comorbidities. Fast-tracking processes with timely recognition and treatment of complications favourably influence patient outcome. Postoperative preventive and therapeutic management has to be carefully planned in order to reduce postoperative morbidity and mortality.

For patients with severe complications, intensive care unit (ICU) mortality rate ranges from 13% to 47%, and hospital mortality ranges from 24% to 65%. Common predictors of in-hospital mortality are severity scores, number of failing organs, general condition, respiratory distress and the need for mechanical ventilation or vasopressors. When considering long-term survival after discharge, cancer-related parameters retain their prognostic value.

Thoracic surgeons, anesthesiologists, pneumologists, intensivists and oncologists need to develop close and confident partnerships aimed at implementing evidence-based patient care, securing clinical pathways for patient management while promoting education, research and innovation. The final decision on admitting a patient with lung to the ICU should be taken in close partnership between this medical team and the patient and his or her relatives.

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Introduction

In Western countries, lung cancer is the primary cause of death by cancer [1], and 8–15% of cancer patients admitted to intensive care units (ICU) have lung cancer [2, 3]. Admission is related to postprocedural/postoperative care, medical complications due to cancer or its treatment and organ failure not related to cancer. The prognosis of ICU cancer patients is determined by acute physiological disturbances leading to intensive care, but not the underlying neoplastic condition [4–6], while survival after recovery is related to the underlying neoplastic disease.

Changes in the management of lung cancer patients, health costs and budgetary constraints induce substantial modifications to ICU usage. Traditionally, surgical lung cancer patients were routinely admitted to the ICU for the immediate postoperative period, but currently we are facing the development of high-dependency (HDU) and post-anaesthesia care units (PACUs). Admitting advanced lung cancer patients to the ICU remains a challenging issue, for which new therapeutic developments with very active targeted therapies have to be taken into account.

This narrative review repositions the current role of the ICU in managing patients with lung cancer, focusing on three major end-points: selection of patients at risk after major surgical procedures; prognosis of lung cancer patients admitted to the ICU; and specific complications leading to ICU admission.

Selection of patients at risk after surgical procedures for ICU admission

Postoperative mortality rates after major thoracic surgical procedures range between 2% and 5%, and cardiopulmonary morbidity between 20% and 40%, resulting in prolonged hospital stays and increased healthcare costs [7].

Post-operative admission to the ICU, HDU or PACU is based on the clinician's judgment for prediction of "avoidable" major complications modulated by available resources. Combining patient- and procedure-related risks approximates the overall risk profile (figure 1).

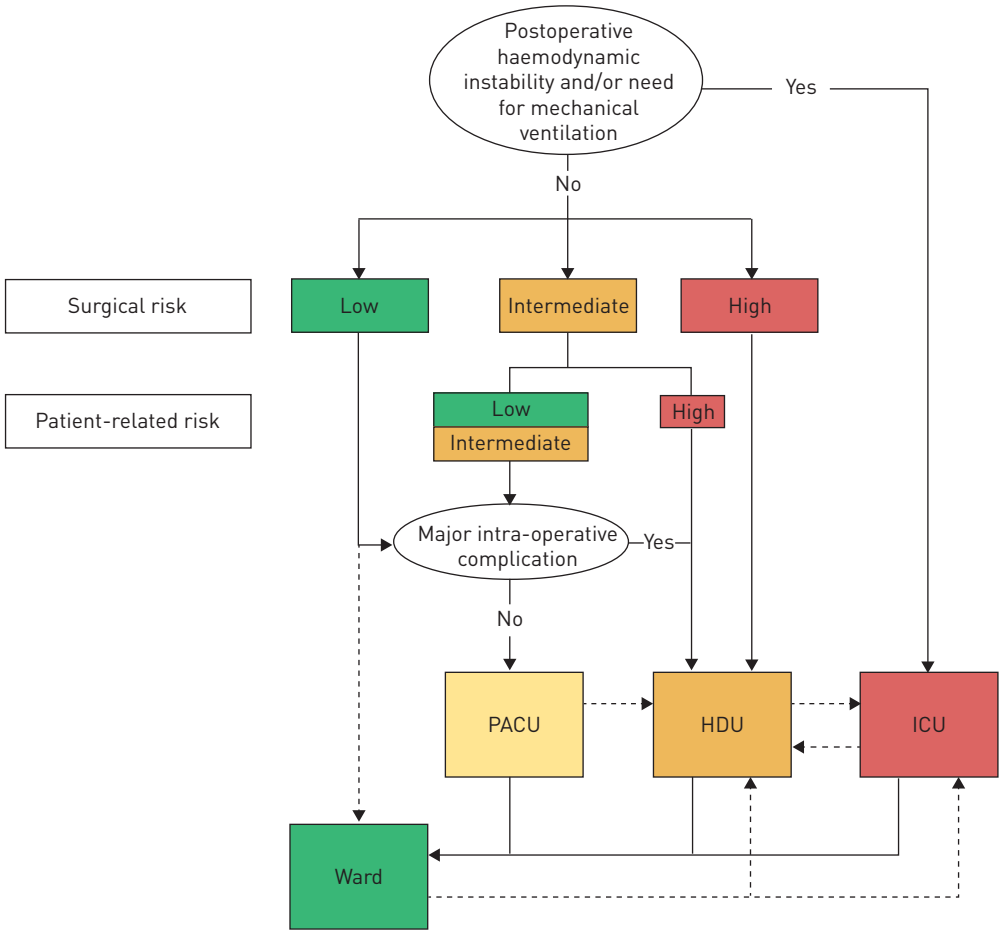

FIGURE 1 Post-thoracotomy patient triage. PACU: post-anaesthesia care unit; HDU: high-dependency unit; ICU: intensive care unit. Reproduced and modified from [7].

TABLE 1 Summary of risk factors indicating a high risk of postoperative complications

Patient-related risk factors	Procedure-related risk factors
ASA physical status ⩾3	High-risk procedure
S-MPM ⩾6 points	Major intraoperative complication[#]
RCRI ⩾2 points	Low level of operator and hospital expertise
ThRCRI >1.5 points	Emergency operation
ARISCAT >45 points	
Preoperative FEV_1 <60%	
ppo-FEV_1 <30%	
ppo-D_{LCO} <30%	
Peak V'_{O_2} <12 mL·kg^{-1}·min^{-1}	
Liver dysfunction[¶]	

ASA: American Society of Anesthesiologists; S-MPM: surgical mortality probability model; RCRI: revised cardiac risk index; ThRCRI: thoracic RCRI; ARISCAT: Assess Respiratory Risk in Surgical Patients in Catalonia risk index; FEV_1: forced expiratory volume in 1 s; ppo: predictive postoperative; D_{LCO}: diffusing capacity of the lung for carbon monoxide; V'_{O_2}: oxygen uptake. [#]: refractory hypotension and/or hypoxaemia, myocardial ischaemia, cardiac arrhythmias requiring treatment, major haemorrhage or bronchial aspiration; [¶]: according to [8–10].

Risk factors for surgical complications and risk stratification

Risk factors are summarised in tables 1, 2 and 3.

Patient-related risk factors

General risk scores

The American Society of Anesthesiologists classification of physical health (ASA) is universally applied for assessing the risk of post-operative morbidity and mortality of patients requiring any surgical, therapeutic or diagnostic procedure. However, high risk (ASA >II) is associated with large interobserver variability and poor specificity, which preclude accurate estimation for individual patients [11].

TABLE 2 Summary of risk scores

ASA		Revised cardiac risk index		Thoracic revised cardiac risk index		ARISCAT risk index	
Risk factors	**Points**	**Risk factors**	**Points**	**Risk factors**	**Points**	**Risk factors**	**Points**
ASA I	0	History of coronary artery disease	1	History of coronary artery disease	1.5	Age: 51–80 years / >80 years	3 / 16
ASA II	2					Respiratory infection in the past month	17
ASA III	4	History of heart failure	1	History of cerebrovascular disease	1.5		
ASA IV	5	History of cerebrovascular disease	1			Surgical incision: upper abdominal / intrathoracic	15 / 24
ASA V	6			Pneumonectomy	1.5		
Surgical risk: low / intermediate / high / emergency intervention	0 / 1 / 2 / 1	High-risk surgery (vascular, intraperitoneal or intrathoracic)	1	Serum creatinine >177 μmol·L^{-1}	1	Emergency procedure	8
						Preoperative S_{pO_2}: 91–95% / ⩽90%	8 / 24
		Preoperative insulin therapy	1			Preoperative anaemia (⩽10 g·dL^{-1})	11
		Serum creatinine >177 μmol·L^{-1}	1			Duration of surgery: >2–3 h / >3 h	16 / 23

ASA: American Society of Anesthesiologists' classification of physical health; ARISCAT: Assess Respiratory Risk in Surgical Patients in Catalonia; S_{pO_2}: arterial oxygen saturation measured by pulse oximetry.

The Charlson comorbidity index (CCI), composed of 19 weighted medical diagnoses, is a valid predictor of 1-year mortality in medical patients; a score >5 being associated with 1-year mortality >50% [12]. Among lung cancer patients undergoing curative resection, a CCI score ⩾3 was associated with a 10-fold greater incidence of major complications [13]. The surgical mortality probability model [14] is used to predict all-cause post-operative mortality at 30 days [15] (tables 2 and 3).

Three further scores, more specifically designed for thoracic surgery, have to be considered. The cardiopulmonary risk index is a combination of cardiac and pulmonary risk factors [16]. The EVAD score utilises pulmonary function test data (forced expiratory volume in 1 s (FEV_1) and diffusing capacity of the lung for carbon monoxide (D_{LCO})) and patient age to predict the likelihood of complications after major lung resection [17]. The "thoracoscore", derived from the French national thoracic surgery database EPITHOR incorporates nine independent risk factors to predict in-hospital mortality [18].

Cardiovascular risk scores

The revised cardiac risk index (RCRI) was developed for prediction of major cardiac complications in nonemergency noncardiac surgery [19] (tables 2 and 3). A RCRI index ⩾3 is associated with major postoperative cardiac complications (+11%). The thoracic RCRI for lung resections was derived from the original RCRI [20] (tables 2 and 3). The predictive power of both scores in patients undergoing lung resections is controversial. More recently, the myocardial infarction and cardiac arrest risk calculator [21] has identified five predictors of perioperative risk at 30 days and provides a more accurate cardiac risk prediction than RCRI, although no data for thoracic surgery are available.

Pulmonary risk scores

Postoperative pulmonary complications (PPCs) are a major cause of morbidity and mortality, possibly accounting for more mortality than cardiovascular complications.

The Assess Respiratory Risk in Surgical Patients in Catalonia (ARISCAT) study established a risk score for the development of PPCs in a cohort of surgical patients based on seven independent risk factors [22] (tables 2 and 3). The score was prospectively and externally validated across many European countries, with a satisfactory predictive power, especially for western European countries [23].

Lung function tests

Dyspnoea is correlated with the risk of postoperative mortality [24]. Standardised symptom-limited climbing of three flights of stairs without interruption is a simple cost-effective test to objectively determine

TABLE 3 Interpretation of risk scores

	Score	Mortality	Score	Risk of major cardiac event	Score	Risk of postoperative pulmonary complications
ASA	1	0.01				
	2	0.02				
	3	0.07				
	4	0.2				
	5	1.5				
	6	4				
	7	10				
	8	25				
	9	50				
Revised cardiac risk index			0	0.4 (0.05–1.5)		
			1	0.9 (0.3–2.1)		
			2	6.6 (3.9–10.3)		
			⩾3	⩾11 (5.8–18.4)		
Thoracic revised cardiac risk index			0	0.9		
			1–1.5	4.2		
			2–2.5	8		
			>2.5	18		
ARISCAT risk index					<26	Low 1.6 (0.6–2.6)
					26–45	Intermediate 13.3 (7.6–19)
					>45	High 42.1 (29.3–54.9)

Data are presented as % or % (95% CI). ASA: American Society of Anesthesiologists classification of physical health; ARISCAT: Assess Respiratory Risk in Surgical Patients in Catalonia.

cardiorespiratory reserve and may have superior predictive ability than traditional spirometry values [7]. Failure to perform this test warrants further lung function testing, while patients able to climb ⩾22 m (five to six flights of stairs) have a low risk of postoperative complications, regardless of lung function test results [25].

A preoperative FEV_1 <70% and a predictive postoperative (ppo) D_{LCO} are reliable predictors of perioperative complications in thoracic surgery [26]. European Respiratory Society/European Society of Thoracic Surgery guidelines use ppo-FEV_1 <30% and ppo-D_{LCO} <30% to discriminates between normal and high-risk groups [7]. However, the calculated ppo-FEV_1 may overestimate the FEV_1 on the first postoperative day by ~30% [27] and patients with a moderate to severe obstructive pulmonary syndrome may improve their respiratory dynamics after lung resection.

Peak oxygen uptake during a standardised effort allows the refinement of perioperative risk prediction, with values >20 $mL \cdot kg^{-1} \cdot min^{-1}$ allowing resection up to pneumonectomy, whereas values <10 $mL \cdot kg^{-1} \cdot min^{-1}$ predict a high risk of any type of lung resection [28] with a mortality rate that may exceed 20% [29].

Age and frailty

Decline in organ function and physiological reserve with ageing is a major risk factor for perioperative morbidity and mortality. Sarcopenia affects muscles of the limbs, respiratory muscles and those controlling the upper airways. Obstructive sleep apnoea and occult aspiration occur more frequently in the context of underlying neurological disorders (*e.g.* previous stroke, dementia or Parkinson's disease) [30]. The risk of postoperative hypoxia and hypercapnia is increased because of altered chemosensitivity, respiratory muscle weakness and increased pulmonary shunting. Impaired thermogenesis favours the occurrence of wound infection, bleeding and cardiac ischaemia, resulting in prolonged postoperative recovery [27]. The risk of postoperative cognitive disorder is increased, especially with benzodiazepine premedication [31].

Frailty is a composite measure of geriatric conditions that may be a valuable aid in determining operability and planning of postoperative care. A multidimensional frailty score including nine items adapted from comprehensive geriatric assessment with a maximal value of 15 has been elaborated for predicting 1-year postoperative mortality [32]. A cut-off score of five allows practitioners to distinguish between high- (mortality >10%) and low-risk populations. Although superior to the ASA score for prediction of 1-year mortality, its computation is time-consuming, and must be performed by a consultant familiar with the score.

Procedure-related risk factors

Lung resections

Thoracic surgery risk assessment focuses primarily on lung resections, particularly in the context of cancer surgery. Broadly, the more extensive the lung resection, the greater the risk of developing postoperative complications (table 4).

The greatest risk is associated with extended pneumonectomy (table 5). Overall, right-sided lung resection carries a higher risk of complications than a left-sided resection, owing to a greater propensity for bronchopleural fistula formation, a greater increase in right ventricular afterload and potential alterations in cardiac sympathicovagal balance [33, 34].

Other thoracic surgical interventions

Interventions requiring single or one-lung ventilation and a thoracotomy expose patients to cardiovascular complications, atelectasis, pneumonia and ventilator-induced lung injuries, leading to acute respiratory distress syndrome (ARDS).

TABLE 4 Risk classification according to type of thoracic surgical procedure

Low risk	Intermediate risk	High risk
Pleural drainage	Bullectomy	Pneumonectomy
Pleurodesis	Pleural resection	Extended lung resection
Mediastinoscopy	Lobectomy	Trachea, bronchial resection
Lung biopsy	Segmentectomy	Mediastinal resections[#]
	Wedge resection	Pneumonectomy
		Pneumonectomy
		Diaphragmatic resection
		Lung volume reduction surgery
		Lung transplantation

[#]: oesophagectomy, mediastinal tumour resection and thymus resection.

TABLE 5 Risk factors according to extent of lung resection

Source [ref.]	Patients n	Mortality	Risk factors
STS GTSD [33]	1267 pneumonectomies	5.6%	Age >65 years, congestive heart failure, FEV_1 <60%, underlying benign lung disease and extended pneumonectomy
French National Database for Thoracic Surgery (EPITHOR) [34]	4498 pneumonectomies	7.8%	Age >65 years, ASA score ⩾3, underweight and right-sided and extended pneumonectomies
STS GTSD [35]	18 800 lung cancer resections	2.2%	Pneumonectomy, bilobectomy, ASA score, functional status, renal dysfunction, induction chemoradiation, steroids, age, urgent procedures, male sex, FEV_1 and body mass index
American National Cancer Database [36]	120 000 patients	Overall 30-day mortality 3.4% for NSCLC resections; 8.5% for pneumonectomies; 4% for extended lobectomies and bilobectomies; 2.6% for lobectomies; 4.2% for wedge resections	

STS: Society for Thoracic Surgeons; GTSD: General Thoracic Surgery Database; FEV_1: forced expiratory volume in 1 s; ASA: American Society of Anesthesiologists' classification of physical health; NSCLC: nonsmall cell lung cancer.

A nomogram was validated to predict the occurrence and severity of postoperative complications after oesophagectomy [35] and proved useful for risk prediction in high-volume hospitals [37]. Independent risk factors are age, history of cerebrovascular or transient ischaemic attack, history of myocardial infarction, reduced FEV_1, ECG changes and extensive surgery.

Lung or pleural biopsies and simple bullectomy with or without pleurodesis using video-assisted thoracic surgery (VATS) require short-term admission to a PACU for monitoring recovery from anaesthesia, lung re-expansion, titration of analgesics and detection of residual air leakage and atelectasis. Mediastinoscopies can generally be monitored in the PACU, with special attention to the risk of occult postoperative haemorrhage.

Additional surgical risk factors

There is little evidence to support the use of a muscle-sparing thoracotomy as opposed to a posterolateral thoracotomy, but incision length may be proportionally related to post-thoracotomy complications [38]. Given limited tissue trauma and consequent reduced neuroendocrine and inflammatory responses, VATS is associated with lower rates of perioperative mortality, morbidity (*e.g.* pneumonia and atrial arrhythmia) and length of stay [34]. In the absence of other major risk factors for postoperative complications, patients with a VATS lung resection are commonly managed in PACUs for monitoring and recovery from anaesthesia.

Operative mortality may be lower if board-certified thoracic surgeons have a minimal case load of procedures [39]. Differences in postoperative mortality rates between hospitals may also be explained by variation in the quality of postoperative patient management [40].

Surgery performed on an emergency basis has repeatedly been associated with worse postoperative outcomes. Various pre- and postoperative scores integrate this factor into risk stratification.

Finally, the occurrence of major intraoperative complications may require a higher level of postoperative monitoring and treatment than initially planned. Myocardial ischaemia, haemodynamically significant arrhythmias, refractory hypotension or hypoxaemia, bronchial aspiration and major bleeding are considered major complications that justify admission to a HDU or ICU.

Anaesthetic management

Improving patient outcome can be achieved by implementing perioperative risk minimisation strategies [8–10]: 1) titration of anaesthetic agents, based on monitoring brain activity; 2) adoption of lung-protective ventilatory settings; 3) control of haemodynamics and achievement of optimal oxygen transport to match metabolic demands (cerebral oxygen saturation by near-infrared spectroscopy); 4) control of normothermia and haemostasis; and 5) efficient pain control.

The type and quality of postoperative pain control influences postoperative triage, since it influences the risk of postoperative cardiopulmonary complications and length of stay [41]. Thoracic epidural analgesia is considered the gold standard for pain management after open thoracic surgery as it has been associated with a lower incidence of postoperative pneumonia and a shorter duration of mechanical ventilation compared to systemic analgesia [42]. Thoracic paravertebral block, performed percutaneously by the anaesthetist or directly by the surgeon, may provide similar analgesia, at lower risk of hypotension and urinary retention [43]. In some institutions, refractory hypotension caused by the thoracic epidural treatment mandates transfer to the HDU or ICU. Over recent decades, the incidence of post-procedural complications has markedly decreased due to the additional benefit of epidural over systemic analgesia [42].

Postoperative selection of patients for ICU, HDU or PACU admission

For most patients, postoperative triage can be planned by taking into account preoperative patient- and procedure-related risk factors while the occurrence of intraoperative complications may modify the initial assessment.

Scores and guidelines

The surgical Apgar score (SAS) includes three intraoperative parameters: blood loss, lowest mean arterial pressure and lowest heart rate, shown to be useful in predicting postoperative major complications or 30-day mortality following noncardiac surgery [44]. So far, thoracic surgical patients have not been included in this exploratory population sample. The SAS has been validated successfully in single centres and in an international study across eight hospitals in eight countries [45]. A score $\geqslant 6$ may signal a high risk of postoperative complications and prompt the clinician to transfer a patient to the HDU or ICU.

The physiological and operative severity score for the enumeration of mortality and morbidity (POSSUM) was developed for audit purposes. It is based on 12 physiological and six operative parameters and allows prediction of in-hospital mortality and morbidity. It proved useful for prediction of postoperative complications in lung-resected patients [46]. Subsequently, the POSSUM score was improved and named Portsmouth-POSSUM (P-POSSUM) [47].

The American College of Critical Care Medicine issued guidelines regarding selection criteria of patients admitted to HDUs [48] and ICUs [49]. Admission to the HDU should be considered for "patients who, after major surgery, are hemodynamically stable, but may require fluid resuscitation and transfusion due to major fluid shifts" and "who require close nurse monitoring during the first 24 h". Admission to the ICU is restricted for a minority of patients requiring "hemodynamic monitoring/ventilatory support or extensive nursing care" (figure 1). Changing the clinical pathway of thoracic surgical patients from the ICU to the PACU and HDU has been shown to be safe and cost-effective [50].

Local characteristics

The spectrum of postoperative units extends from day care and surgical wards to PACUs, HDUs and ICUs. Every hospital has a unique combination of postoperative units, staffing, expertise and technical equipment, which greatly influence postoperative triage decisions. Triage guidelines must therefore be adjusted to those characteristics, and developed by a local multidisciplinary team composed of surgeons, anaesthetists, pneumologists and intensivists.

In some institutions, all postsurgical patients are first transferred to the PACU before being transferred either to the ward or to the HDU. This offers more clinical information at the time of the final triage, since the first postoperative hours are a period of major physiological variation with the potential appearance of early pathological processes.

A transfer to the ward entails a substantial decrease in the quality and frequency of monitoring. The provision of a medical emergency team composed of anaesthetists and/or intensivists, may be a way to attenuate the risk [51] and may influence postoperative triage decisions.

Prognosis of the lung cancer patient admitted to the ICU

Series including mostly stage III–IV lung cancer have shown that the prognosis of lung cancer patient admitted to the ICU improved substantially with time. Before 2005, very high ICU mortality rates (46–85%) were consistently reported; currently these have decreased to 13–47% [52]. Hospital mortality rates followed a similar decline from 75–91% to 24–65% [52]. However, we have to consider a possible selection bias, as arguments from pulmonologists and oncologists to admit patients to the ICU, as well as those advanced by intensivists to refuse them, could have changed during these periods in parallel to the introduction of new, more active anticancer treatments and improvement in intensive care management.

Studies assessing prognostic factors are heterogeneous and of limited size. Among 13 studies, only seven included >100 patients [52]. The most frequently reported independent prognostic factors during ICU stay appeared to be performance status, acute respiratory failure, number of failing organs and need for vasopressors or mechanical ventilation. In addition, neoplastic airways obstruction, acute respiratory failure, cancer status, comorbidities, severity scores, sepsis and renal failure were predictive for in-hospital mortality. When long-term mortality was assessed, the cancer characteristics (presence of metastasis and cancer progression) retained their prognostic value.

Roques *et al.* [53] showed, in 105 lung cancer patients requiring ICU stay, a 6-month mortality rate of 73%; two-thirds of survivors received anti-cancer treatment. Toffart *et al.* [54] showed that 3-month and 1-year survival rates were 37% and 12%, respectively. A worsening of organ dysfunction at 72 h after ICU admission was associated with higher mortality (45% *versus* 8% if organ dysfunction improved). 3-month survival was independent of noninvasive ventilation (NIV) requirement (40% *versus* 47% without NIV), but was significantly decreased in patients requiring endotracheal intubation (22%). For patients discharged alive from the ICU, the median survival after discharge was 104 days, the estimated survival being 54% at 90 days and 18% at 1 year.

The SEER (Surveillance, Epidemiology, and End Results) register analysed 49 373 lung cancer patients admitted to the ICU for reasons other than surgical resection [55]. Of these, 76% survived the hospitalisation and 35% were alive 6 months after discharge. Hospital mortality increased when mechanical ventilation was given, with 6-month survival only 15%. A second study performed on the same database focused on 1134 patients aged >65 years with stage IIIB and IV nonsmall cell lung cancer (NSCLC) [56]. Mortality rates at 90 days and at 1 year were 71% and 90%, respectively, with an in-hospital mortality rate of 33%. Among patients discharged alive, 42% returned home while the others were transferred to rehabilitation services or palliative care institutions. Only 19% of patients received cancer treatment after hospital discharge.

Specific complications and ICU management

Surgical complications

Even with optimal surgical and anaesthetic techniques, morbidity remains substantially elevated. Predominantly cardiac, pulmonary and pleural complications may arise in up to 83% of patients after extrapleural pneumonectomy with pericardial and diaphragmatic reconstruction [57]. Although minimally invasive procedures can be performed in high-risk patients with a lower complication rate, pre-existing clinical factors may be responsible for severe postoperative complications, justifying a close interaction between intensivists, anaesthetists, pneumologists, cardiologists, thoracic surgeons, medical oncologists and physiotherapists in the postoperative period.

Cardiac arrhythmias

Supraventricular tachyarrhythmias are more common than ventricular rhythm disturbances after noncardiac thoracic surgery [58]. Atrial fibrillation typically occurs between the second and fourth postoperative day in 10–20% of patients after lobectomy, but in up to 40% after pneumonectomy [59]. Significant risk factors are right pneumonectomy, intrapericardial dissection, advanced age and reduced fluid intake. Adequate monitoring for several days is recommended and extensive guidelines are available from the American Association for Thoracic Surgery [60].

Respiratory complications

Pulmonary oedema is reported in up to 9% of patients after pneumonectomy and in 1–5% after lesser resection, with a high mortality rate [61, 62]. It is a noncardiogenic, noninfectious pulmonary oedema that is considered to be a postresectional form of ARDS characterised by permeability oedema and diffuse alveolar damage. Therapy follows of the old adage "keep the patient dry"; reintubate or apply noninvasive ventilation in cases of respiratory failure along with the administration of inotropic/vasopressive drugs, while restricting fluid intake [63].

Postpneumonectomy syndrome is caused by extreme mediastinal shifting. Patients complain of progressive dyspnoea due to airway and vascular compression. In severe cases tissue expanders are used to reposition the mediastinum towards the midline [64].

Orthodeoxia–platypnoea syndrome is characterised by dyspnoea in a sitting position and is less pronounced when the patient lies down. It is related to reopening of a patent foramen ovale with an intracardiac shunt. A closing device can be used to obliterate the shunt [65].

Thromboembolic disease (either deep vein thrombosis or complicated by pulmonary embolism) is favoured by the hypercoagulability state induced by the cancer. Its incidence is up to 15% in lung cancer

patients [66] and 1–5% in surgical patients [67]. Prevention by use of low molecular weight heparin, elastic stockings and early ambulation is of utmost importance. In high-risk patients the use of pneumatic compression devices is recommended. Management is not different from other thromboembolic diseases, except that it must be pursued for as long as the risk factor persists. Treatment modalities have switched over time to low molecular weight heparin [67, 68]; recently, in medical patients, direct oral anticoagulants have been demonstrated to be equally effective [69], but are not yet standard practice. For patients with severe haemodynamic compromise, thrombolytic therapy or pulmonary embolectomy may be applied.

Prolonged air leak is a common problem in patients with emphysema, which was reported in up to 50% of cases, rendering it the most frequent postoperative complication. Air leak is considered to be abnormal when it persists after 5 days [70]. Progressive subcutaneous and mediastinal emphysema may develop, eventually resulting in swollen face and eyes, the so-called "Michelin syndrome". Risk factors include severe bullous emphysema, lung volume reduction surgery and prolonged ventilatory support giving rise to barotrauma. Perioperative control of the bronchial stump and staple lines is recommended, if necessary by applying fibrin glue or other sealants, by reinforcement with strips or the creation of a pleural tent by detaching the parietal pleura. In a Cochrane systematic review, surgical sealants reduced postoperative air leaks and time to chest tube removal; however, a significant reduction in length of hospital stay could not be demonstrated [71]. Postoperatively, patients should be extubated as soon as possible to reduce the intrapulmonary pressure. Injection of talc, other sclerosing agents or autologous blood may be helpful to close a persisting parenchymal air leak. Insertion of a pigtail catheter with a Heimlich valve allows ambulatory treatment. For difficult cases, intrabronchial valves have been proposed to close alveolar pleural fistulas [72].

Lobar torsion is an uncommon (<0.5%), but dramatic complication [73, 74]. It occurs by the twisting of a remaining lobe around its bronchovascular pedicle, mainly, but not exclusively within the right middle lobe [75], with haemorrhagic infarction and lung necrosis. Diagnosis is obtained by bronchoscopy [76], and in most cases a completion pneumonectomy is needed. Prevention by fixation of the remaining lobe/s to surrounding tissue during the initial procedure is indicated [75].

Specific pleural complications

Persistent pleural space or a residual space, described as a "persisting pneumothorax" by thoracic radiologists, is observed after major lung resection less than after pneumonectomy. So-called "complicated residual spaces" are present when there is a persisting air leak or when colonisation with bacteria or fungi occur, giving rise to a pleural empyema. Drainage of the remaining pleural cavity is indicated [77]. Muscle flaps may be used to fill up the residual space in order to prevent recurrent infection. Pleural empyema is a rare event after lobectomy, but occurs in 2–12% of pneumectomies and is often associated with a bronchopleural fistula [73]. Risk factors include cardiovascular and pulmonary comorbidities, older age, malnutrition, neoadjuvant or induction therapy, diabetes, steroids, right pneumonectomy and extended resection, postoperative ARDS, pneumonia and prolonged mechanical ventilation. Pleural fluid culture before starting antibiotics is needed to detect the responsible bacteria and/or fungi, and antibacterial or antifungal treatment adapted as necessary. Initial therapy includes complete drainage of the pleural space in combination with antibiotics or antimycotics. Irrigation of the pleural space with an antiseptic solution may be necessary [78], and sometimes a temporary or definitive thoracostomy may be required to control a severe infection [79].

Bronchopleural fistula implies a direct communication between a remaining bronchial stump and the pleural space [80]. Clinical symptoms are quite similar to those of empyema and it is often heralded by a progressive inflammatory syndrome and respiratory distress. Massive expectoration of dark brown fluid may occur in the case of large fistula. Early cases are observed within 7 days of the procedure and are usually caused by inadequate or incomplete closure of the bronchial stump. Late cases are related to failure of healing of the bronchial stump, recurrent disease or progressive endobronchial or endotracheal infection. Risk factors are quite similar to empyema. Perioperative measures preventing bronchopleural fistula include covering of the bronchial stump with viable tissue [81]. Bronchoscopy is indicated to inspect the bronchial suture or staple line. Smaller fistulas may be detected by the injection of methylene blue at the stump. Management is similar to empyema and multidisciplinary collaboration is required for adequate treatment [82]. In cases of sudden expectoration of a large volume of fluid, the patient should be positioned with the head elevated and operated side down. Smaller fistulas may sometimes be obliterated bronchoscopically by the injection of glue or a sclerosing agent. Surgical closure of a larger bronchopleural fistula should be attempted after resolution of pleural infection, with excision of all necrotic tissue and covering of the remaining bronchial stump with viable tissue as a muscle flap, pericardium or omentum [73]. Postoperative irrigation of the thoracic cavity is indicated to prevent a recurrent empyema or fistulisation.

Specific interventions of intensive care in thoracic oncology (other than surgical complications)

Respiratory problems are the second most frequent cause of ICU admission in lung cancer patients [83]. The following events are commonly reported: febrile neutropenia and poststenotic infection (retro-obstructive pneumonia) (not addressed here), dyspnoea and acute respiratory failure, generally associated with pneumothorax or haemoptysis.

Pneumothorax

During the period of cancer staging, most ICU admissions are related to adverse events following tumour sampling. Transthoracic needle biopsies are complicated by pneumothoraxes in up to 60% of cases, but only a minority (up to 15%) requires pleural drainage or admission to critical care [84]. Transbronchial biopsies have a lower incidence of complications [85]. Pneumothorax can appear a few hours after the procedure despite normal postprocedural radiography, which must be repeated. Pneumothorax may occur spontaneously due to tumour invasion or necrosis after chemotherapy. Severe respiratory failure is rare in the absence of other comorbidities, and pleural drainage is rapidly effective. Prolonged air leak is managed similarly to the postoperative setting.

Intrabronchial bleeding

Endoscopic biopsies rarely result in severe bleeding if standard precautions are taken: withholding anticoagulants and platelet antiaggregants, with the exception of low-dose aspirin. Massive haemoptysis can result from tumour infiltration or parenchymal necrosis following poststenotic infections, but rarely from thromboembolism. Haemoptysis from tumour growth is generally moderate, but massive bleeding due to the involvement of large vessels such as pulmonary arteries can occur. Admission to the ICU is recommended when bleeding is significant (>200 mL per 24 h or >50 mL per episode) or is responsible for respiratory distress (need for supplemental oxygen >4–5 $L \cdot min^{-1}$ or arterial oxygen saturation measured by pulse oximetry <88%) or haemodynamic instability. Patients receiving anticoagulation and those who have extensive tissues necrosis but are potentially amenable to surgery should also be admitted. The diagnostic workup consists of a chest computed tomography scan and a bronchoscopy if the exact origin of the bleeding is unknown. Treatment modalities are oxygen administration and selective intubation in cases of massive bleeding. Bronchoscopy, preferably rigid bronchoscopy under general anaesthesia, can be used to coagulate intrabronchial lesions or to ensure proper selective intubation. Bronchial artery embolisation may sometimes be of limited value or have a transient effect. Surgery is sometimes feasible, but mortality is high. Antifibrinolytics are of limited, if any, use. In the absence of contraindications (mainly cardiac ischaemia and uncontrolled hypertension), vasopressin analogues show some effectiveness while waiting for interventional bronchoscopy, embolisation or surgery.

Acute airway obstruction

Acute obstruction of major airways arises in central tumours, due to intraluminal tumour growth, extraluminal compression or a mixed mechanism. With a few exceptions (severely functionally impaired patients), only tracheal or bilateral proximal obstructions generate significant respiratory distress. Dyspnoea is generally progressive, but can sometimes be acute, with stridor or wheezing depending on the level of obstruction. Ablation of the intraluminal tumoural component can be obtained by various techniques (laser, electrocoagulation or mechanical removal) if a visible lumen persists, followed by the implantation of endoluminal stents. Distal patent bronchi and normal lung are needed for insuring benefit. The procedure is performed under rigid bronchoscopy and general anaesthesia [86, 87].

Major pericardial and pleural fluid effusions

Intrathoracic malignancies regularly metastasize to pleura and/or pericardium, resulting in respiratory/cardiac impairment [88]. With few exceptions, related to massive intracavitary bleeding the symptoms are progressive and are treated either by direct puncture (pleural/pericardial) or by drainage. Repeated puncture should be avoided since it poses a significant infectious risk and pleurodesis and/or pericardial drainage should be performed as soon as possible.

Some aetiologies of major dyspnoea

Rarely, dyspnoea can result from glottic oedema in the case of superior vena cava syndrome. The treatment relies on intravascular stenting and anticoagulation to prevent the extension of intracaval thrombosis. Corticosteroids and diuretics are ineffective [89]. Radiotherapy is not an emergency treatment, despite its potential effectiveness.

Progressive dyspnoea is frequently related to diffuse pulmonary involvement by lymphangitic or local spread. There is no specific therapy (including corticosteroids) showing activity outside of anticancer treatment, and ICU management relies only on administration of oxygen. Those patients should only be

admitted to ICU if an active anticancer treatment can be provided [90]. Interstitial pneumonia may be related to side-effects of some tyrosine kinase inhibitors (TKIs). Sometimes, the cause of respiratory distress is difficult to pinpoint and more than one mechanism is involved. As these patients have frequent cardiac comorbidities, an *N*-terminal pro-brain natriuretic peptide dosage can be ordered to rule out a cardiac aetiology [91].

Advanced lung cancer and systemic anticancer treatment during ICU stay

Prognosis of advanced lung cancer has changed over time with the introduction of new active chemotherapeutic agents, and for small subpopulations, very active targeted agents. Nevertheless, facing a persisting disease with poor prognosis, a few predictive factors for hospital mortality, including pre-existing poor performance status and weight loss, have to be considered before ICU admission [54, 92]. Other factors to be considered before ICU admission are the reversibility of the acute complication, such as desobstruction of proximal airways, therapeutic options for the lung cancer to be delivered after resolution of the acute complication, the absence of neoplastic progression [54] and the wishes of the patient. In a recent prospective study, Toffart *et al*. [83] showed that the absence of refusal from the patients or their relatives is an independent factor for ICU referral.

Interest in administering anticancer treatment in ICU remains controversial, except for high-risk therapy (high-dose methotrexate, risk of severe allergic reaction, *etc.*). The level of evidence concerning the role of (urgent) chemotherapy in ICU is low, and most series deal with a mixed population, predominantly with haematological malignancies [93]. All studies demonstrated the feasibility of administering conventional chemotherapy, despite reduced prognosis for solid tumours [93, 94]. Prognostic factors reflect organ dysfunction (need for vasopressors, mechanical ventilation, hepatic failure and sequential organ failure assessment score [93–95].

Specific data for lung cancer are very limited. In a series of 20 small cell lung cancer (SCLC) patients, five received chemotherapy during their ICU stay [96]. Only two survived for >200 days. However, the introduction of targeted therapies with a rapid and very high response rate changed our pessimistic view, with case reports [97, 98] suggesting major activity of TKIs in patients with oncogenic driver mutations and respiratory failure, who were also on mechanical ventilation. The largest retrospective case–control study [90] included 14 patients with epidermal growth factor receptor mutation or anaplastic lymphoma kinase or ROS-1 rearrangements. Despite hospital mortality of 50%, those patients with activating mutations receiving TKIs had reduced 30-day mortality ($p=0.07$) and better survival (hazard ratio 0.12, $p=0.002$) than historical controls.

Due to its recent introduction into the armamentarium, there are no adequate data on immunotherapy and intensive care. However, by stimulating the immune system, these agents should probably be used with caution in patients presenting with modified immune systems (systemic inflammatory response syndrome, neutropenia, *etc.*).

Some indications for radiotherapy during ICU stay resulted from small series suggesting that irradiation for intubated patients could be beneficial. In a series of 26 patients (21 NSCLC, four SCLC), seven patients were extubated and six were discharged alive from the hospital [99].

Administering anticancer treatment in the ICU justifies an extensive discussion between the intensivist, the oncologist and patients or their relatives, taking into account the balance of benefit and risk. Specific populations with activating mutations should probably have more benefit in this setting with very active targeted therapies.

Conclusion

Patients with lung cancer will face intensive care management for two main reasons: postoperative setting or acute complications, related or not to their cancer or its treatment.

Careful preoperative assessment is mandatory to reduce postoperative morbidity and mortality. The anaesthetist plays a major role in decreasing postoperative risk and reducing the need for high-level postoperative monitoring. The trend for moving thoracic surgical postoperative care from the ICU towards HDUs or PACUs depends on the patient, procedure-related risk factors and on local specificities.

Severe cardiac and respiratory complications are the most common complications leading to ICU admission. Prevention and early recognition, as well as interdisciplinary cooperation are essential to obtain the best outcome [79]. Urgent anticancer treatment in patients suffering from respiratory failure due to tumoural infiltration yielded some success, mainly in cases of activating mutations/rearrangement, and should be discussed on a case-by-case basis.

Although prognosis may be poor, admission to the ICU should be proposed to lung cancer patients after discussion between the patient and the multidisciplinary team, taking into account the possibility of reversal of the acute complication and the anticancer therapeutic options to be delivered during or after the ICU stay.

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