



ORIGINAL ARTICLE

Factors associated with short- and long-term outcomes in lung cancer patients requiring unplanned invasive mechanical ventilation



Emeric Chatelain^a, Marie Simon^a, Romain Hernu^a, Laurent Argaud^{a,b}, Martin Cour^{a,b,*}

^a Hospices Civils de Lyon, Hôpital Edouard Herriot, Service de Médecine Intensive-Réanimation, F-69437, Lyon, France

^b Université de Lyon, Université Claude Bernard Lyon 1, Faculté de Médecine Lyon-Est, F-69373, Lyon, France

Received 29 March 2023; accepted 7 July 2023

Available online 6 October 2023

KEYWORDS

Lung cancer;
Mechanical ventilation;
Intubation;
Ventilator weaning;
Long-term prognosis

Abstract

Objective: Unplanned invasive mechanical ventilation (IMV) is associated with high mortality in lung cancer patients. We aimed to identify factors associated with weaning from IMV, intensive care unit (ICU) survival and 1-year survival in lung cancer patients requiring unplanned IMV.

Design: Retrospective observational study (2007–2017).

Setting: University-affiliated ICU.

Patients: Lung cancer patients requiring unplanned IMV.

Intervention: None.

Main variables of interest: Weaning from IMV, ICU and 1-year survival.

Results: Of the 136 patients included in the analysis (age 64 (9) years, male 110 (81%), metastatic disease 97 (62%)), 52 (38%) were weaned from IMV, 51 (38%) were discharged from ICU and 22 (16%) were alive at 1 year. The main indication for intubation was acute respiratory failure. In multivariate analysis, PaO₂/FiO₂ >175 mmHg at ICU admission and intubation before ICU admission were associated with successful weaning from IMV while intubation for cardiac arrest was associated with weaning failure. Same factors were associated with ICU survival. Absence of metastasis at ICU admission and lung resection surgery were independently associated with 1-year survival.

Abbreviations: ARDS, acute respiratory distress syndrome; ARF, acute respiratory failure; CCI, Charlson Comorbidity Index; CI, confidence interval; COPD, chronic obstructive pulmonary disease; ICU, intensive care unit; IMV, invasive mechanical ventilation; NIV, non-invasive ventilation; OR, odds ratio; SAPSII, Simplified Acute Physiology Score II; SD, standard deviation; SOFA, Sequential Organ Failure Assessment.

* Corresponding author at: Hospices Civils de Lyon, Hôpital Edouard Herriot, Service de Médecine Intensive-Réanimation, F-69437, Lyon, France.

E-mail address: martin.cour@chu-lyon.fr (M. Cour).

<https://doi.org/10.1016/j.medine.2023.07.014>

2173-5727/© 2023 Elsevier España, S.L.U. and SEMICYUC. All rights reserved.

Conclusions: A significant proportion of patients with lung cancer treated with unplanned IMV could be weaned from IMV and survived to ICU discharge, especially in the absence of severe hypoxemia at ICU admission. The low one-year survival was mostly driven by metastatic status. © 2023 Elsevier España, S.L.U. and SEMICYUC. All rights reserved.

PALABRAS CLAVE

Cáncer de pulmón;
Ventilación
mecánica;
Intubación;
Destete ventilatorio;
Pronóstico a largo
plazo

Factores asociados a los resultados a corto y largo plazo en pacientes con cáncer de pulmón que requieren ventilación mecánica invasiva no planificada

Resumen

Objetivo: La ventilación mecánica invasiva (VMI) no planificada se asocia a una elevada mortalidad en pacientes con cáncer de pulmón. El objetivo de nuestro estudio fue identificar los factores asociados con el destete de la VMI y la supervivencia en unidad de cuidados intensivos (UCI) y a 1 año en pacientes con cáncer de pulmón que requieren VMI no planificada.

Diseño: Estudio observacional retrospectivo (2007–2017).

Ámbito: UCI universitaria.

Pacientes: Pacientes con cáncer de pulmón que requirieron VMI no planificada.

Intervención: Ninguna.

Variables de interés principales: Destete de la VMI y supervivencia a 1 año.

Resultados: Se incluyeron 136 pacientes: edad 64(9) años, sexo masculino 110 (81%), enfermedad metastásica 97 (62%). De ellos, 52 (38%) fueron destetados de la VMI. La supervivencia en UCI y al año era 38% (n=51) y 16% (n=22) respectivamente. La principal indicación de intubación fue la insuficiencia respiratoria aguda. En el análisis multivariante, la PaO₂/FiO₂ >175 mmHg al ingreso en la UCI y la intubación realizada antes del ingreso en la UCI se asociaron a un destete satisfactorio de la VMI, mientras que la intubación por parada cardíaca se asoció a un fracaso del destete. Los mismos factores se encontraron para la supervivencia en UCI. La ausencia de metástasis al ingreso en la UCI y la cirugía de resección pulmonar se asociaron de forma independiente con la supervivencia a 1 año.

Conclusiones: Una proporción significativa de pacientes con cáncer de pulmón tratados con VMI no planificada pueden ser destetados de la VMI, especialmente en ausencia de hipoxemia grave al ingreso en UCI. La baja supervivencia a un año se debió principalmente al estado metastásico. © 2023 Elsevier España, S.L.U. y SEMICYUC. Todos los derechos reservados.

Introduction

Lung cancer is the second most common cancer worldwide and remains the leading cause of cancer-related deaths, with nearly 2 million deaths each year.¹ Admissions of lung cancer patients to the intensive care unit (ICU) are frequent, and 20–80% of these patients are treated with invasive mechanical ventilation (IMV), which is associated with a very high short-term mortality rate.^{2–6} Unplanned intubation in patients with lung cancer occurs in emergency situations and frequently occurs before ICU admission. The patient's wishes regarding intensive care and oncologic prognosis are often unknown at the time of intubation.⁷ Thus, the level of care and therapeutic goals should be discussed as soon as possible after the initiation of IMV. Even in cases where short- or medium-term prognosis is poor because of cancer, weaning from IMV is an acceptable therapeutic goal. Indeed, removal of the endotracheal tube can improve patient comfort. In the most favorable cases, patients are discharged from the ICU and continue oncological treatments.^{2,4,5,8} However, most reports indicate that the weaning process fails in a majority of these patients.^{2,5,6,9,10} Thus, ICU care

is often considered as “futile” in this setting.¹¹ Therefore, it is important to identify the factors associated with successful weaning from IMV and long-term survival in patients with lung cancer requiring unplanned intubation. This would help to provide adequate prognostic information to patients or relatives and/or to prevent unnecessary life-prolonging therapy in ICU. The primary endpoint was to identify factors associated with weaning success in lung cancer patient requiring unplanned IMV. We also aimed to identify the independent factors associated with ICU survival and 1-year survival.

Patients and methods

Study design

We conducted a retrospective cohort study of patients with lung cancer requiring unplanned IMV from 2007 to 2017. The study received approval from the regional ethics committee with a waiver for written informed consent because of the retrospective nature of the study. The study was conducted

in compliance with the ethical standards detailed in the 1964 Declaration of Helsinki. Non-opposition for the use of anonymous data for research purposes was obtained during the ICU stay.

Patients

All adult patients with active lung cancer or in remission for less than 5 years requiring unplanned IMV and admitted to our 15-bed university-affiliated medical ICU were included.

Data collection

The following variables were collected for each patient: age, gender, comorbidities, body mass index (BMI), source of admission (home or hospital), Charlson Comorbidity Index (CCI),¹² and performance status¹³ assessed in the week prior to ICU admission.

The following lung cancer features were recorded: histological type, follow-up in an oncologic reference center, metastatic disease as defined in the 8th version of TNM classification,¹⁴ targetable driver mutation (EGFR, ALK, ROS1), time since cancer diagnostic, anticancer treatment before ICU admission. The cancer status was determined for each patient at the time of admission and classified as follows: newly diagnosed (treatment not yet started), newly treated (treatment started for less than 2 months or without oncologic re-evaluation), progression/recurrence, remission (for less than 5 years).

The main indication for IMV and the place of intubation were collected. Simplified Acute physiology Score II (SAPS II) was recorded¹⁵ as well as Sequential Organ failure Assessment (SOFA) score evaluated at 24 and 72 h from admission.¹⁶ The ratio of partial oxygen pressure to oxygen inspired fraction ($\text{PaO}_2/\text{FiO}_2$) was used to describe the severity of acute respiratory failure (ARF) at ICU admission (in the case of several values, the worst was considered). Acute respiratory distress syndrome (ARDS) was defined according to the Berlin definition.¹⁷

The use of non-invasive ventilation (NIV) before intubation and the duration of IMV were recorded. Weaning failure was defined as the need for reintubation or death within 48 h following weaning from IMV.¹⁸ Other interventions were collected during the ICU stay including paralyzing agents, prone positioning, renal replacement therapy, use of vasopressors and anti-cancer chemotherapy in ICU. End-of-life decisions were recorded. Continuation of cancer treatment after ICU discharge, hospital discharge, survival at 6 months and at 1 year were also collected.

Statistical analysis

Values are presented as mean (standard deviation, SD) or number (%), as appropriate. Univariate comparisons were performed using MannWhitney *U* test for continuous variables and Fisher's exact test for categorical variables, as appropriate. Backward stepwise multivariate analysis using a logistic regression model was performed to assess the factors predicting successful extubation and survival in ICU. Following univariate analysis, clinically relevant variables

with $p \leq 0.10$ were included in the model. Potential confounding factors were eliminated if $p > 0.10$. Odds ratios (OR) were estimated with 95% confidence intervals (95% CI). When needed, quantitative variables were transformed into dummy variables according to their median. Because of the collinearity with $\text{PaO}_2/\text{FiO}_2$ ratio at admission, the SAPS II, SOFA score, and ARDS variables were not included in the model. Also, because targetable driver mutations were sought in a limited number of patients, this variable was not included in the model.

The independent contribution to mortality by parameters possibly influencing the 1-year outcome was tested by a backward stepwise multivariate Cox proportional hazard model, using time to death as the dependent variable. In addition, we introduced age in the model to avoid retaining confounding factors related to this major demographic covariate. Hazard ratios (HR) were estimated with 95% CI.

To assess the potential influence of time, patient characteristics and outcomes were compared between 2 consecutive periods: 2007–2011, 2012–2017.

GraphPad Prism 9.0 software (GraphPad Software, CA, USA) and WizardPro (version 1.9 29) were used to perform statistical analysis. A *p* value < 0.05 value was considered statistically significant.

Results

Population

One hundred thirty-six patients were included in this study (Table 1). Half of the patients were followed up in an oncologic reference center, and two-thirds had metastatic disease (Table 1). The most common histological type of cancer was adenocarcinoma (46%). A targetable driver mutation was present in 5 patients, including 4 EGFR-activating mutations and 1 ALK rearrangement. Eleven patients were treated with targeted therapies (erlotinib ($n=9$), osimertinib ($n=1$), and crizotinib ($n=1$)), and three received nivolumab.

In most cases, the patients were admitted to the ICU from their homes or via the emergency room (Table 2). The main indication for intubation was ARF, mainly due to pneumonia (including 6 pneumocystis pneumoniae), followed by cancer-related complications (12 tracheobronchial obstructions and atelectasis, 5 pulmonary lymphangitic carcinomatosis, 5 hemoptysis, 4 pleural effusions, 1 superior vena cava syndrome, 1 radiation-induced lung injury, and 1 tumor lysis syndrome). Intubation was performed before ICU admission in more than 50% of cases (Table 2). Among the 112 (78%) patients with ARDS, neuromuscular blocking agents were used in 22 (26%) and prone positioning in 4 (3%). Most patients had extrapulmonary organ failure and received vasopressors.

Weaning from IMV and survival in ICU

Fifty-two patients (38%) were successfully weaned from IMV (Tables 1 and 2). All these patients except one were discharged alive from ICU. Weaning from IMV success rate did not differ between the 2 predefined periods of the study ($p=NS$). The proportion of patients with chronic renal fail-

Table 1 Baseline characteristics.

	All (n = 136)	Weaned (n = 52)	Unweaned (n = 84)	p
Demographics				
Age, years	64 (9)	63 (9)	64 (9)	0.40
Male gender	110 (81%)	41 (79%)	69 (82%)	0.80
Body mass index, kg m ⁻²	24 (5)	23 (4)	24 (5)	0.14
Comorbidities				
COPD	60 (44%)	26 (50%)	34 (40%)	0.36
Coronary artery disease	28 (21%)	14 (27%)	14 (17%)	0.22
Diabetes mellitus	34 (25%)	13 (25%)	21 (25%)	>0.99
Chronic renal failure	8 (6%)	7 (13%)	1 (1%)	<0.01
Charlson Comorbidity Index	8 (3)	8 (3)	8 (2)	0.45
Performance status				
0–1	70 (51%)	34 (65%)	36 (43%)	0.01
2 or more	65 (48%)	18 (35%)	48 (57%)	
Lung cancer				
Follow-up in reference center	70 (51%)	29 (56%)	41 (49%)	0.48
Time since cancer diagnosis, days	271 (432)	344 (548)	225 (336)	0.23
Time since last treatment, days	115 (265)	160 (331)	82 (204)	0.59
Cancer histological type				0.51
Adenocarcinoma	63 (46%)	24 (46%)	39 (46%)	
Squamous cell carcinoma	26 (19%)	9 (17%)	17 (20%)	
Small cell lung cancer	22 (16%)	11 (21%)	11 (13%)	
Other	18 (13%)	6 (11%)	12 (14%)	
Unknown	7 (5%)	2 (4%)	5 (6%)	
Metastatic disease	92 (67%)	31(60%)	61 (72%)	0.13
Targetable driver mutation	5 (4%)	4 (8%)	1 (1%)	0.07
Anticancer treatment				
Chemotherapy/targeted therapy	76 (56%)	29 (56%)	47 (56%)	>0.99
Lung resection	21 (15%)	12 (23%)	9 (11%)	0.09
Radiation	39 (29%)	15 (29%)	24 (29%)	>0.99
Not yet started	44 (32%)	16 (31%)	28 (33%)	0.85
Number of treatment lines				
0–1	105 (77%)	42 (81%)	63 (75%)	0.69
2 or more	31 (23%)	10 (19%)	21 (25%)	
Cancer status				
Remission	47 (35%)	21 (40%)	26 (31%)	0.61
Newly diagnosed	44 (32%)	16 (31%)	28 (33%)	
Newly treated	12 (9%)	5 (10%)	7 (8%)	
Recurrence / Progression	33 (24%)	10 (19%)	23 (27%)	

Data are expressed as mean (SD) or number (%).

COPD: Chronic obstructive pulmonary disease.

ure, with performance status at 0–1, intubated prior to admission, and intubated for neurological failure, as well as the SOFA score and PaO₂/FiO₂ ratio, were significantly different in patients who were weaned from IMV or not (Tables 1 and 2). None of the 6 patients diagnosed with pneumocystis could be weaned from IMV.

In multivariate analysis, PaO₂/FiO₂ >175 mmHg (i.e., median value of the cohort) at ICU admission and intubation before ICU admission were associated with successful weaning from IMV while cardiac arrest was associated with weaning failure (Table 3). The factors associated with survival in the ICU were the same as those associated with weaning from IMV (Table 3).

One-year survival

The mortality rates in the ICU, hospital, and 6 months and 1 year after ICU admission were 62%, 71%, 79%, and 84%, respectively. One-year mortality rate was not significantly different between the 2 predefined periods of the study (p=NS). Most deaths occurred within 1 month after ICU admission (Fig. 1). End-of-life decisions were reported in 75 (55%) patients, on average 6 (8) days after ICU admission. These decisions were significantly more frequent (p<0.01) in the unweaned group than in the weaned group (66/82 (80%) vs. 9/54 (17%)). The factors associated with one-year mortality after ICU admission are summarized in Table 4.

Table 2 Organ failure and treatments in ICU.

	All (n = 136)	Weaned (n = 52)	Unweaned (n = 84)	p
Source of admission				0.86
Home/Emergency room	76 (56%)	30 (57%)	46 (54%)	
General hospital	60 (44%)	22 (42%)	38 (45%)	
Indication for intubation				
Pulmonary sepsis	59 (43%)	23 (44%)	36 (43%)	>0.99
Cancer related events	30 (22%)	8 (15%)	22 (26%)	0.20
Cardiac arrest	16 (12%)	1 (2%)	15 (18%)	<0.01
Neurological failure	15 (11%)	11 (21%)	4 (5%)	<0.01
Non-respiratory sepsis	7 (5%)	3 (6%)	4 (5%)	>0.99
Surgical adverse events	7 (5%)	4 (8%)	3 (4%)	0.43
Cardiogenic pulmonary edema	2 (1%)	2 (4%)	0 (0%)	0.14
SAPS II	61 (21)	58 (15)	64 (24)	0.30
SOFA score at ICU admission				
Respiratory	2.8 (1.1)	2.2 (1.1)	2.8 (0.9)	<0.01
Cardiovascular	2.9 (1.7)	2.8 (1.8)	3.0 (1.7)	0.32
Renal	0.6 (1.0)	0.5 (0.9)	0.6 (1.0)	0.59
Coagulation	0.4 (0.9)	0.2 (0.6)	0.5 (1.0)	0.03
Hepatic	0.1 (0.5)	0.1 (0.3)	0.1 (0.6)	0.76
Neurological	1.3 (1.6)	1.3 (1.6)	1.3 (1.6)	0.86
Total	7.8 (3.1)	7.0 (2.6)	8.3 (3.3)	0.02
Acute respiratory failure				
PaO ₂ /FiO ₂ at admission, mmHg	195 (105)	240 (119)	168 (85)	<0.01
ARDS at inclusion	112 (82%)	37 (71%)	75 (89%)	0.01
ICU treatments				
Invasive mechanical ventilation				
Started before ICU admission	76 (56%)	35 (67%)	41 (56%)	0.05
Started after NIV failure	34 (25%)	13 (25%)	21 (25%)	0.13
Duration, days	7.8 (8.0)	7.4 (7.5)	8.1 (8.3)	0.90
Renal replacement therapy	10 (7%)	2 (4%)	8 (10%)	0.37
Vasopressors	106 (78%)	38 (73%)	68 (81%)	0.29
Chemotherapy	8 (6%)	3 (6%)	5 (6%)	0.99

Data are expressed as mean (SD) or number (%).

SAPS II: Simplified Acute Physiology Score II; SOFA: Sequential Organ Failure Assessment; ICU: Intensive care unit; PaO₂/FiO₂: arterial partial pressure of oxygen to fraction of inspired oxygen; ARDS: Acute respiratory distress syndrome; NIV: noninvasive ventilation.

Table 3 Factors independently associated with successful weaning from invasive mechanical ventilation and ICU survival.

	Odds ratio	95% CI	p
Weaning from IMV			
Cardiac arrest	0.045	0.005–0.376	0.004
IMV started before ICU admission	2.347	1.052–5237	0.037
PaO ₂ /FiO ₂ at admission >175 mmHg	3.704	1.674–8196	<0.001
ICU survival			
Cardiac arrest	0.048	0.006–0.401	0.005
IMV started before ICU admission	2.279	1.021–5086	0.044
PaO ₂ /FiO ₂ at admission >175 mmHg	3.354	1.515–7426	0.003

CI confidence interval; IMV: invasive mechanical ventilation; ICU: intensive care unit; PaO₂/FiO₂: arterial partial pressure of oxygen to fraction of inspired oxygen.

Cumulative mortality at 1 year was significantly ($p < 0.05$ by log-rank test) higher in patients who had metastasis, no lung resection surgery, cardiac arrest and low PaO₂/FiO₂ ratios (Fig. 2). In multivariate analysis, absence of metasta-

sis at ICU admission (HR 0.57, 95%CI [0.39–0.82]; $p < 0.01$) and lung resection surgery (HR 0.62, 95%CI [0.38–0.99]; $p < 0.05$) were independently associated with 1-year mortality rate.

Table 4 Characteristics of survivors and non-survivors at 1 year after ICU admission.

	Survivors(n = 22)	Non-survivors(n = 114)	p
Demographics			
Age, years	62 (9)	64 (9)	0.96
Male gender	15 (68%)	95 (83%)	0.17
Body mass index, kg m ⁻²	24 (4)	23 (5)	0.85
<i>Performans status</i> 0 or 1	15 (68%)	55 (48%)	0.22
Lung cancer			
Time since cancer diagnosis, days	444 (743)	237 (336)	0.10
Cancer histological type			0.91
Non-small cell lung cancer	16 (73%)	91 (80%)	
Small cell lung cancer	4 (18%)	18 (16%)	
Unknown	2 (9%)	5 (4%)	
Metastatic disease	9 (41%)	83 (73%)	< 0.01
Targetable driver mutation	3 (14%)	2 (2%)	0.03
Lung resection	7 (32%)	14 (12%)	0.045
Treatment lines <2	20 (91%)	85 (75%)	0.61
Cancer status			0.33
Remission	10 (45%)	37 (32%)	
Active	12 (55%)	77 (68%)	
Indication for intubation			
Pulmonary sepsis	10(45%)	49 (43%)	>0.99
Cancer related events	4 (18%)	26 (23%)	0.78
Cardiac arrest	0 (0%)	16 (14%)	0.07
Neurological failure	4 (18%)	11 (10%)	0.27
Non-respiratory sepsis	0 (0%)	7 (6%)	0.59
Surgical adverse events	3 (14%)	4 (4%)	0.08
Cardiogenic pulmonary edema	1 (5%)	1 (1%)	0.30
SAPS II	55 (17)	62 (22)	0.17
SOFA score at admission	6.8 (2.7)	8.0 (3.2)	0.86
PaO ₂ /FiO ₂ at admission, mmHg	248 (135)	185 (96)	0.01
ICU treatments			
Renal replacement therapy	1 (5%)	9 (8%)	0.92
Vasoactive drugs	14 (64%)	81 (71%)	0.61
Chemotherapy	2 (9%)	6 (5%)	0.84

Data are expressed as mean (SD) or number (%).

SAPS II: Simplified Acute Physiology Score II; SOFA: Sequential Organ Failure Assessment; PaO₂/FiO₂: arterial partial pressure of oxygen to fraction of inspired oxygen; ICU: Intensive care unit.

Oncologic care during and after ICU stay

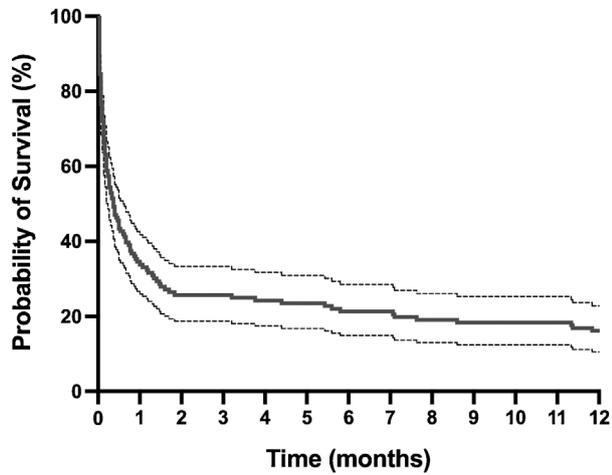
Emergency chemotherapy was performed in eight (6%) patients, all of whom had newly diagnosed small cell lung cancer. No targeted therapy was started in ICU. Of the 36 ICU survivors with planned cancer treatment, 23 (64%) received cancer treatment after ICU stay. For patients with a targetable driver mutation, one died in the ICU, one in the month following ICU admission, and three were still alive at 1 year.

Discussion

This study found that more than one-third of lung cancer patients with unplanned IMV could be weaned from the ventilator, and identified that patients who were not intubated before ICU admission, with severe hypoxemia, and/or with cardiac arrest were less likely to be weaned from IMV. None of the factors related to lung cancer

independently influenced the weaning success. Conversely, one-year mortality was only driven by factors related to lung cancer (metastatic status and no lung cancer resection).

Data on weaning success in patients with lung cancer requiring unplanned IMV are scarce.^{9,10,19} In the present study, we found that 38% of patients were successfully weaned off the ventilator. This figure is much higher than the previously reported 15% (7/46) reported by Ewer et al. in 1986.¹⁰ Nevertheless, patients were at a higher risk of weaning failure, as they all had active lung cancers versus 65% in our study. A study published approximately 20 years later reported a closer success rate of extubation (27%) in 81 lung cancer patients treated with IMV for ARF.⁹ More recently, in a selected population of lung cancer patients with EGFR mutations treated with tyrosine kinase inhibitors as a first-line therapy, weaning from unplanned IMV was successful in twice as many patients as in our study.¹⁹ These latter results are in line with our own, since four of the five patients (80%) in our cohort treated with targeted therapy



N. at risk 136 48 37 37 31 27 22

Figure 1 One-year survival curve.

Panel A represents the one-year survival curve of the 136 patients with lung cancer requiring unplanned invasive mechanical ventilation. The dashed lines indicate 95% confidence intervals.

could be weaned from IMV. Nevertheless, these patients still represent a minority of those managed in the ICU.⁴

In the present study, the severity of hypoxemia at admission was the main factor associated with weaning from IMV. This result is consistent with those of previous studies on oncologic patients with or without lung cancer.^{4,10,19,20} The poor prognosis related to respiratory failure in patients with lung cancer could be explained by the fact that the causes of hypoxemia are, in many cases, poorly reversible (e.g., proximal tumoral airway obstruction, lymphangitic carcinomatosis, smoking-related pulmonary diseases). In our cohort, delayed IMV (from ICU admission) was also associated with a higher risk of weaning failure. In line with our findings, previous studies reported that late initiation of IMV or IMV initiation after NIV failure was a poor prognostic factor in cancer patients with ARF.^{20,21} Interestingly, in our study, weaning from IMV was not associated with cancer characteristics. Nevertheless, there was a limited number of patients with proximal airway obstruction, which is an important prognostic factor in other studies.^{2,22} Finally, we identified cardiac arrest as the cause of unplanned IMV as an independent factor for weaning failure. Given the very poor prognosis of patients with asphyxia-induced cardiac arrest in the general population,²³ this finding is not surprising.

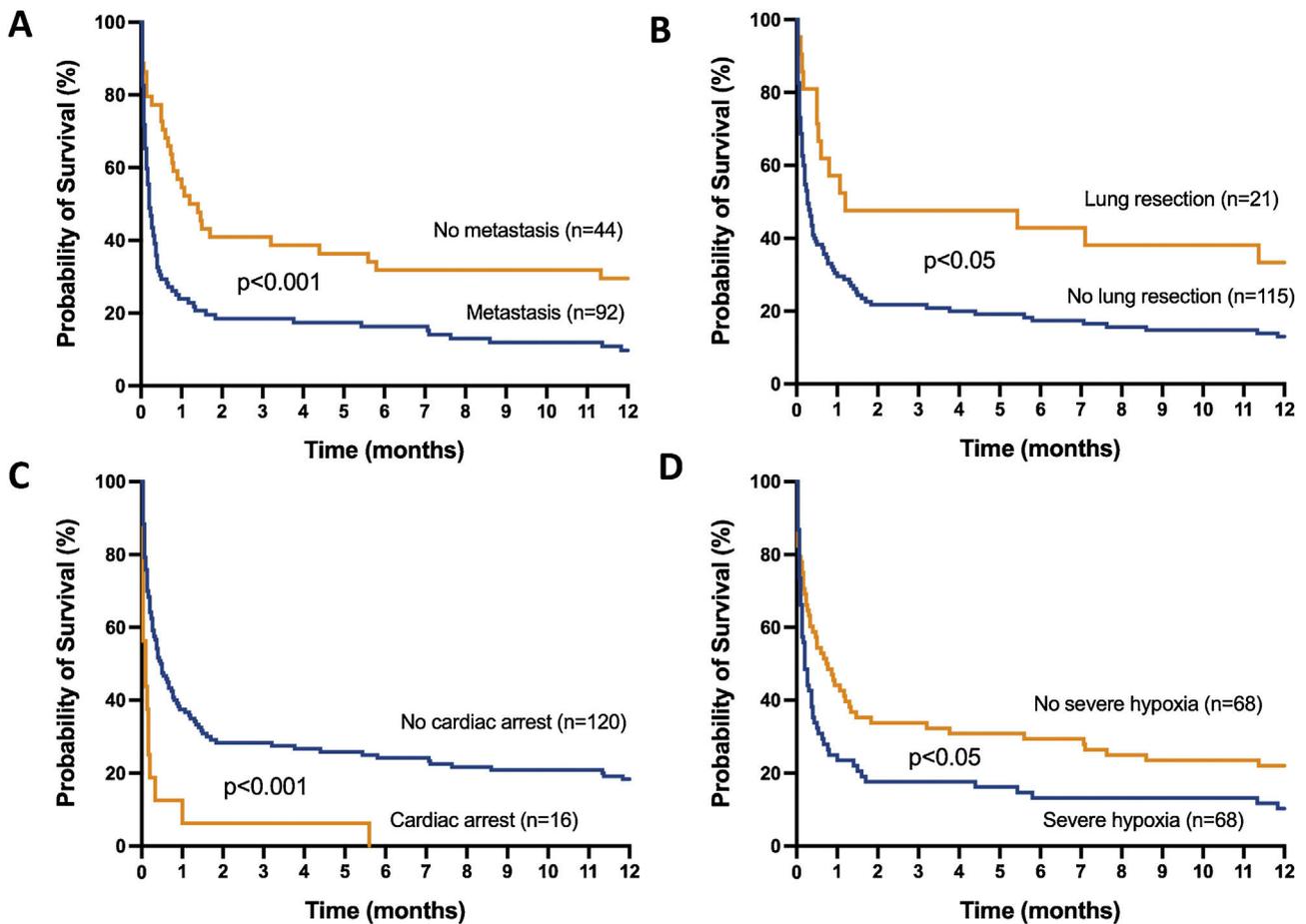


Figure 2 Kaplan-Meier plots showing representative factors influencing probability of survival.

Metastasis (A), absence of lung resection as a treatment for lung cancer (B), cardiac arrest as the reason for invasive mechanical ventilation (C) and severe hypoxemia (i.e., $PaO_2/FiO_2 \leq 175$ mmHg) at intensive care unit admission (D), were associated ($p < 0.05$ by the log-rank test) with a significantly higher rate of mortality.

In the last two decades, the outcomes of oncological patients requiring intensive care have improved.^{10,19–21,24} Nevertheless, the 1-year mortality of patients with lung cancer admitted to the ICU and receiving or not receiving IMV remains as high as 70%.⁴ Early data on the mortality of lung cancer patients requiring unplanned IMV reported a mortality rate of approximately 90%.^{9,10} However, recent data are lacking. In the present study, we reported a slightly lower 1-year mortality rate (84%). Nevertheless, our cohort included patients with a better prognosis at baseline than those in previous studies,^{9,10} as it included patients in remission and IMV for causes other than respiratory failure. Apart from the severity of hypoxemia at ICU admission, the 2 factors independently associated with 1-year outcomes were related to lung cancer characteristics (metastatic status and lung cancer resection). This finding is consistent with prior studies showing that metastasis and/or cancer progression and the use of IMV for ARF are the most important predictive factors of poor long-term outcomes.^{4,21,22,25} Knowledge of these prognostic factors is important to discuss the level of therapeutic commitment in close collaboration with the oncologist, especially for patients with advanced disease.^{26,27} Another important element to consider is the possibility of resuming or continuing oncological treatment (when indicated) after ICU discharge. This was the case for more than half of the patients included in our study, suggesting that unplanned IMV only moderately compromises the continuation of essential oncological treatments. This finding confirms those of previous studies that included a large proportion of patients who did not receive IMV.^{5,8,28}

This study has several limitations. First, this study analyzed data from patients admitted to the ICU over a long period of time (11 years), ending in 2017, whereas the prognosis of cancer patients requiring ICU care improved during the study period. Nevertheless, the patient characteristics and outcomes did not change over time. This is in line with a recent study that showed no change in mortality between 2007 and 2018 in lung cancer patients admitted to the ICU for life-threatening complications.⁴ Second, there were a limited number of patients for whom targetable mutations were assessed, and only 11 (8%) patients received targeted therapy. Third, we included a heterogeneous population of patients with different cancer stages and long-term prognosis.

In conclusion, our study highlights that a significant proportion of lung cancer patients treated with unplanned IMV can be weaned from IMV, especially in the absence of severe hypoxemia at ICU admission. Most eligible patients received further oncological treatment after ICU discharge. However, one-year mortality was very high and was mostly driven by metastatic status. These results would help provide adequate prognostic information to relatives and/or prevent unnecessary life-prolonging therapy in the ICU.

Authors' contribution

EC and MC participated in the acquisition, analysis and interpretation of data and drafted the manuscript. MC performed the statistical analyses. MS and RH participated in acquisition of data and were involved in revising the manuscript critically. LA participated in the design and coordination of

the study, helped to draft the manuscript. All authors read and approved the final version of the manuscript.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors

Competing interests

All the authors declare they have no competing interests.

References

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of incidence and mortality worldwide for 36 cancers in 185 Countries. *CA A Cancer J Clin*. 2021;71:209–49, <http://dx.doi.org/10.3322/caac.21660>.
2. Slatore CG, Cecere LM, LeTourneau JL, O'Neil ME, Duckart JP, Wiener RS, et al. Intensive care unit outcomes among patients with lung cancer in the surveillance, epidemiology, and end results–medicare registry. *J Clin Oncol*. 2012;30:168691, <http://dx.doi.org/10.1200/JCO.2011.40.0846>.
3. Lung Cancer in Critical Care (LUCCA) Study Investigators, Barth C, Soares M, Toffart AC, Timsit JF, Burghi G, et al. Characteristics and outcome of patients with newly diagnosed advanced or metastatic lung cancer admitted to intensive care units (ICUs). *Ann Intensive Care*. 2018;8:80, <http://dx.doi.org/10.1186/s13613-018-0426-2>.
4. Vigneron C, Charpentier J, Wislez M, Mira J-P, Lefebvre A, Fournel L, et al. Short-term and long-term outcomes of patients with lung cancer and life-threatening complications. *Chest*. 2021;160:1560–4, <http://dx.doi.org/10.1016/j.chest.2021.04.056>.
5. Andréjak C, Terzi N, Thielen S, Bergot E, Zalcman G, Charbonneau P, et al. Admission of advanced lung cancer patients to intensive care unit: a retrospective study of 76 patients. *BMC Cancer*. 2011;11:159, <http://dx.doi.org/10.1186/1471-2407-11-159>.
6. Benguerfi S, Dumas G, Soares M, Meert AP, Martin-Loeches I, Pene F, et al. Etiologies and outcome of patients with solid tumors admitted to ICU with acute respiratory failure: a secondary analysis of the EFRAIM study. *Respir Care*. 2023;68:740–8, <http://dx.doi.org/10.4187/respcare.10604>.
7. Serey K, Cambriel A, Pollina-Bachelier A, Lotz J-P, Philippart F. Advance directives in oncology and haematology: a long way to go - a narrative review. *J Clin Med*. 2022;11:1195, <http://dx.doi.org/10.3390/jcm11051195>.
8. Roques S, Parrot A, Lavole A, Ancel P-Y, Gounant V, Djibre M, et al. Six-month prognosis of patients with lung cancer admitted to the intensive care unit. *Intensive Care Med*. 2009;35:2044–50, <http://dx.doi.org/10.1007/s00134-009-1625-y>.
9. Ewer MS. Outcome of lung cancer patients requiring mechanical ventilation for pulmonary failure. *JAMA*. 1986;256:3364–6, <http://dx.doi.org/10.1001/jama.1986.03380240058028>.
10. Lin Y-C, Tsai Y-H, Huang C-C, Hsu K-H, Wang S-W, Tsao TC-Y, et al. Outcome of lung cancer patients with acute respiratory failure requiring mechanical ventilation. *Respir Med*. 2004;98:43–51, <http://dx.doi.org/10.1016/j.rmed.2003.07.009>.
11. Temel JS, Greer JA, Muzikansky A, Gallagher ER, Admane S, Jackson VA, et al. Early palliative care for patients with metastatic non-small-cell lung cancer. *N Engl J Med*. 2010;363:733–42, <http://dx.doi.org/10.1056/NEJMoa1000678>.

12. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis.* 1987;40:373–83, [http://dx.doi.org/10.1016/0021-9681\(87\)90171-8](http://dx.doi.org/10.1016/0021-9681(87)90171-8).
13. Oken MM, Creech RH, Tormey DC, Horton J, Davis TE, McFadden ET, et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. *Am J Clin Oncol.* 1982;5:649–56, <http://dx.doi.org/10.1097/00000421-198212000-00014>.
14. Asamura H, Nishimura KK, Giroux DJ, Chansky K, Hoering A, Rusch V, et al. IASLC lung cancer staging project: the new database to inform revisions in the ninth edition of the TNM classification of lung cancer. *J Thorac Oncol.* 2023;18:564–75, <http://dx.doi.org/10.1016/j.jtho.2023.01.088>.
15. Le Gall JR. A new Simplified Acute Physiology Score (SAPS II) based on a European/North American multicenter study. *JAMA.* 1993;270:2957–63, <http://dx.doi.org/10.1001/jama.270.24.2957>.
16. Cour M, Klouche K, Souweine B, Quenot JP, Schwebel C, Perinel S, et al. Remote ischemic conditioning in septic shock: the RECO-Sepsis randomized clinical trial. *Intensive Care Med.* 2022;48:1563–72, <http://dx.doi.org/10.1007/s00134-022-06872-1>.
17. Hanley C, Giacomini C, Brennan A, McNicholas B, Laffey JG. Insights regarding the Berlin definition of ARDS from prospective observational studies. *Semin Respir Crit Care Med.* 2022;43:379–89, <http://dx.doi.org/10.1055/s-0042-1744306>.
18. Béduneau G, Pham T, Schortgen F, Piquilloud L, Zogheib E, Jonas M, et al. *Am J Respir Crit Care Med.* 2017;195:772–83, <http://dx.doi.org/10.1164/rccm.201602-03200C>.
19. Lee I-H, Yang C-Y, Shih J-Y, Yu C-J. Tyrosine kinase inhibitors improved survival of critically ill EGFR-mutant lung cancer patients undergoing mechanical ventilation. *Biomedicines.* 2021;9:1416, <http://dx.doi.org/10.3390/biomedicines9101416>.
20. Azoulay É, Thiéry G, Chevret S, Moreau D, Darmon M, Bergeron A, et al. The prognosis of acute respiratory failure in critically ill cancer patients. *Medicine.* 2004;83:360–70, <http://dx.doi.org/10.1097/01.md.0000145370.63676.fb>.
21. Cantón-Bulnes ML, Jiménez-Sánchez M, Alcántara-Carmona S, Gimeno-Costa R, Berezo-García JA, Beato C, et al. Determinants of mortality in cancer patients with unscheduled admission to the Intensive Care Unit: a prospective multicenter study. *Med Intensiva.* 2022;46:669–79, <http://dx.doi.org/10.1016/j.medin.2021.08.005>.
22. Soares M, Darmon M, Salluh JIF, Ferreira CG, Thiéry G, Schlemmer B, et al. Prognosis of lung cancer patients with life-threatening complications. *Chest.* 2007;131:840–6, <http://dx.doi.org/10.1378/chest.06-2244>.
23. Argaud L, Cour M, Dubien P-Y, Giraud F, Jossan C, Riche B, et al. Effect of cyclosporine in nonshockable out-of-hospital cardiac arrest: The CYRUS randomized clinical trial. *JAMA Cardiol.* 2016;1:557–65, <http://dx.doi.org/10.1001/jamacardio.2016.1701>.
24. Shimabukuro-Vornhagen A, Böll B, Kochanek M, Azoulay É, von Bergwelt-Baildon MS. Critical care of patients with cancer. *CA Cancer J Clin.* 2016;66:496–517, <http://dx.doi.org/10.3322/caac.21351>.
25. Boussat S, El'rini T, Dubiez A, Depierre A, Barale F, Capellier G. Predictive factors of death in primary lung cancer patients on admission to the intensive care unit. *Intensive Care Med.* 2000;26:1811–6, <http://dx.doi.org/10.1007/s001340000701>.
26. Borcoman E, Dupont A, Mariotte E, Doucet L, Joseph A, Chermak A, et al. One-year survival in patients with solid tumours discharged alive from the intensive care unit after unplanned admission: a retrospective study. *J Crit Care.* 2020;57:36–41, <http://dx.doi.org/10.1016/j.jcrr.2020.01.027>.
27. Benoit DD, van der Zee EN, Darmon M, Reyners AKL, Metaxa V, Mokart D, et al. Outcomes of ICU patients with and without perceptions of excessive care: a comparison between cancer and non-cancer patients. *Ann Intensive Care.* 2021;11:120, <http://dx.doi.org/10.1186/s13613-021-00895-5>.
28. Soares M, Toffart A-C, Timsit J-F, Burghi G, Irrazábal C, Pattison N, et al. Intensive care in patients with lung cancer: a multinational study. *Ann Oncol.* 2014;25:1829–35, <http://dx.doi.org/10.1093/annonc/mdu234>.