Original Article

Characteristics, management, and outcomes of patients with lung cancer admitted to a tertiary care intensive care unit over more than 20 years

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Abstract:

RATIONALE: The prognosis of patients with lung cancer admitted to the intensive care unit (ICU) is often perceived as poor. We described the characteristics, management, and outcomes of critically ill patients with lung cancer and determined the predictors of mortality.

METHODS: We retrospectively studied patients with lung cancer who were admitted to the ICU of a tertiary care hospital between 1999 and 2021 for the reasons other than routine postoperative care. We noted their characteristics, ICU management, and outcomes. We performed the multivariable logistic regression analysis to determine the predictors of hospital mortality.

RESULTS: In the 23-year period, 306 patients with lung cancer were admitted to the ICU (median age = 63.0 years, 68.3% males, 45.6% with moderate/severe functional disability, most had advanced lung cancer, and median Acute Physiology and Chronic Health Evaluation II score = 24.0). Life support measures included invasive mechanical ventilation (47.1%), vasopressors (34.0%), and new renal replacement therapy (8.8%). Do-Not-Resuscitate orders were implemented during ICU stay in 30.1%. The hospital mortality was 43.8% with a significantly lower rate in patients admitted after 2015 (28.0%). The predictors of mortality were moderate/severe baseline disability (odds ratio [OR] 2.65, 95% confidence interval [CI] 1.22, 5.78), advanced lung cancer (OR 8.36, 95% CI 1.81, 38.58), lactate level (OR 1.45, 95% CI 1.12, 1.88, invasive mechanical ventilation (OR 10.92, 95% CI 4.98, 23.95), and admission period after 2015 (OR 0.37, 95% CI 0.16, 0.85).

CONCLUSIONS: The mortality rates in patients with lung cancer admitted to the ICU during a 23-year period decreased after 2015. Functional disability, advanced lung cancer stage, vasopressor use, and invasive mechanical ventilation predicted mortality.

Keywords:

Goals of care, intensive care, lung cancer, mechanical ventilation, mortality

Lung cancer, its treatment, and the accompanying comorbidities often lead to respiratory and nonrespiratory illnesses that may require intensive care unit (ICU) admissions. Lung cancer, one of the common cancers, is the leading cause of cancer deaths worldwide and has a significant economic burden.[1-3] It is commonly classified into two histologic categories: Small cell lung cancer (SCLC) and non-small lung cancer (NSCLC). The latter represents the vast majority of cases and is further subdivided into three main types in the order of increasing incidence: Adenocarcinoma, squamous cell carcinoma, and large cell carcinoma.[4] Cancer subtype, stage and location along with the patient's

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preferences, comorbidities, and fitness for surgery are important to determine which treatment option is most appropriate.[5] Patients in early stages may benefit from surgical resection, adjuvant chemotherapy, stereotactic ablative body radiotherapy, or percutaneous radiofrequency ablation, while chemotherapy with platinum-based drugs is used for treating advanced stages.[5] The discovery of key somatic mutations, such epidermal growth factor receptor and Kirsten rat sarcoma mutations, and anaplastic lymphoma kinase, as therapeutic targets has allowed personalized treatment regimens, especially in advanced cases of NSCLC.[5]

The causes of ICU admission include hemoptysis, airway obstruction, malignant pleural effusion, pneumonia, exacerbation of chronic obstructive pulmonary disease, myocardial infarction, and pulmonary edema.[6-8] Many of these conditions can lead to acute respiratory failure and requirement for ventilator support as well as other organ dysfunction.[8-10] In a study of 100 patients with advanced or metastatic lung cancer, acute respiratory failure, septic and cardiogenic shock, as well as cardiac arrest were the primary reasons for admission, among those 75% presented with complications related to their lung cancer, mainly airway obstruction.[6]

Patients with lung cancer were historically considered poor candidates for ICU admission due to high mortality rates.[10] However, recent studies show an improvement in the outcome of cancer patients admitted to the ICU.[11] Studies reported mortality rates close to 80% before 2000,[12] but became close to 60% in the first decade of the 21 century[13,14] and went down to close to 40% in the second decade.[8] However, there is the variation in the reported mortality rates between centers.[15] A multicenter study of 449 patients in 22 ICUs in six countries in Europe and South America during 2011 demonstrated an overall hospital, 30-day, and 6-month mortality rates of 39%, 41%, and 55%, respectively.[8] Predictors of mortality in patients with lung cancer requiring ICU admission include older age, the severity of organ dysfunction, poor performance status, recurrent and/or progressive cancer, and metastatic disease.[8-10]

This study aimed at assessing the characteristics and outcomes of patients with lung cancer admitted to the ICU and evaluate the predictors of mortality and having a do-not-resuscitate order during ICU stay.

Methods

Study design, setting, and patients

This was a retrospective study of all adult patients with a diagnosis of lung cancer who were admitted between January 1, 1999, and December 31, 2021, to the ICUs of a 1400-bed tertiary care referral hospital in Riyadh, Saudi Arabia. The intensive care department had multiple ICUs that functioned as closed units and were covered by onsite intensivists and registrars 24 h per day, 7 days per week.[16] According to the hospital policy, patients with an established treatment limitation (such as those with do-not-resuscitate orders) were not admitted to the ICU. The goals of care were addressed in the ICU as per the discretions of the treating medical team. According to the hospital policy, a do-not-resuscitate order could be instituted if three qualified physicians agreed that the prognosis of the patient was poor after discussion with the patient or surrogate decision maker.[17] In case of no acceptance, full support was provided in the vast majority of cases. An ethics committee was available for consultation.

After 2016, medical oncology patients, including those with lung cancer, were preferentially admitted to a newly established cancer center and its oncology ICU. In this study, we included all adult patients with lung cancer who were admitted to any adult ICU and excluded patients who were admitted to the ICU postoperatively after lung cancer resection. For patients who had more than one admission to the ICU during the same hospitalization, only the first ICU admission was analyzed.

The Institutional Review Board of the Ministry of National Guard Health Affairs approved the study and waived informed consent.

Data collection

We noted the characteristics, ICU management, and outcomes of the study patients. The patient characteristics included age, sex, body mass index, chronic illnesses (cardiac, respiratory, renal, hepatic, diabetes, and hypertension), smoking history, Modified Rankin Scale,[18] histological type of lung cancer (NSCLC with its subtypes, SCLC, and other histologies), cancer stage at the time of cancer diagnosis and ICU admission, presence of gene mutation or oncogenes, pre-admission treatment (chemotherapy, radiation, and surgery), duration between diagnosis and ICU admission (months), admission type (medical vs. surgical), admission Glasgow Coma Scale, admission Acute Physiology And Chronic Health Evaluation (APACHE II),[19] the lowest ratio of arterial oxygen partial pressure to fractional inspired oxygen (PO_2:FiO_2) on day of admission, and laboratory findings (platelet count, creatinine, lactate, international normalized ratio, and admission period categorized into these periods 1999–2005, 2006–2010, 2011–2015, and after 2015). The studied management aspects were vasopressor use within 24 h of admission, noninvasive ventilation, intubation and mechanical

ventilation, new renal replacement therapy for acute kidney injury, tracheostomy, and change the level of treatment from full support to do-not-resuscitate order during ICU stay. The primary outcome of this study was hospital mortality. The secondary outcomes were ICU mortality, duration of mechanical ventilation, length of stay in the ICU and hospital, and the diagnosis of venous thromboembolism (deep-vein thrombosis or pulmonary embolism) during hospital stay by limb ultrasound or chest computed tomography angiography.

Statistical analysis

We categorized patients into two groups (survivors and nonsurvivors) depending on their vital status at hospital discharge. We presented the frequencies of categorical variables with percentages and compared between-group differences using the Chi-square test or Fisher's exact test. We presented the medians of continuous data with their interquartile ranges (IQRs) and compared between-group differences using the Student's *t*-test or Mann–Whitney *U*-test depending on the normality of distribution. As this study spanned more than 20-year period, we assessed changes in hospital mortality in four different admission periods (1999–2005, 2006–2010, 2011–2015, and 2016–2020) in all patients and in patients with a higher probability of death in the hospital (patients who received mechanical ventilation, had stage IV NSCLC or had do-not-resuscitate orders).

We performed stepwise multivariable logistic regression analysis (backward elimination using the likelihood ratio test) to determine the predictors of having a do-not-resuscitate order and of hospital mortality. Independent variables entered in the model were selected based on clinical significance and included age, sex, body mass index, preexisting chronic comorbidities (Hypertension, diabetes, and chronic cardiac, respiratory, kidney, and liver diseases), preadmission functional status (moderate/severe vs. normal/mild functional disability based on the modified Rankin scale), advanced lung cancer (NSCLC stage IV and SCLC with extensive stage), admission APACHE II score, creatinine, lactate, international normalized ratio, vasopressor use, the requirement for invasive mechanical ventilation, and admission period (1999–2015 vs. 2016 and after). In the model, we imputed the missing values for the continuous variables (body mass index, APACHE II score, creatinine, lactate, and international normalized ratio) by the respective median. We presented the results as odds ratios (ORs) with 95% confidence intervals (CIs).

Statistical Package for the Social Sciences software version 15 (SPSS Inc, Chicago, USA) was used for the data analysis. Statistical significance for all the tests was set at a $P < 0.05$.

Results

Baseline characteristics of all patients

During the 23-year study period, 306 patients with lung cancer were admitted to adult ICUs. The characteristics of these patients are presented in Table 1. Their median age was 63.0 years (IQR 56.0, 72.0); the majority were males 68.3%; and comorbid conditions were common (hypertension 46.1%, diabetes 37.9%, chronic respiratory diseases 25.2%, and chronic cardiac diseases 21.2%). 45.7% had moderate-to-severe disability at baseline. For patients with known histopathology, 206/239 patients (86.2%) had NSCLC (149/239 adenocarcinoma and 42/239 squamous cell carcinoma). Most patients had advanced disease at the time of diagnosis and at the time of ICU admission (171/200 patients with NSCLC [85.5%] had stage IV and all the 20 patients with SCLC had extensive stage).

Patients admitted to the ICU after 2015 had similar age compared with those admitted between 1999 and 2015 (64.0 ± 12.0 years vs. 61.7 ± 14.8 years, respectively; $P = 0.13$), but had a lower rate of advanced lung cancer (128/158 [81.0%] vs. 66/66 [100%], $P < 0.0001$). Gene mutations were tested in 77 patients (in only one patient before 2016).

Management in the intensive care unit

Table 2 shows the key interventions performed while in the ICU. Almost one-third of patients (34.0%) needed vasopressors and one-tenth (8.8%) had new renal replacement therapy for AKI. Out of 170 patients with data on the use/no use of noninvasive ventilation, 91 received this treatment (53.5%) with 41 patients (44.0%) eventually intubated. Among the whole cohort, almost one-half of patients (47.1%) received invasive mechanical ventilation. Tracheostomy was performed in 16/306 patients (5.2%).

Do-not-resuscitate orders were instituted in 91/302 patients (30.1%) during the ICU stay. Multivariable logistic regression analysis found the following factors to be significantly associated with a do-not-resuscitate order: Diabetes (OR 2.58, 95% CI 1.15, 5.70), chronic cardiac disease (OR 2.58, 95% CI 1.04, 6.39), advanced lung cancer (OR 11.57, 95% 1.29, 103.7), invasive mechanical ventilation (OR 9.88, 95% CI 3.83, 25.51), and admission period after 2015 (OR 0.26, 95% CI 0.12, 0.59).

Patients admitted after 2015 had lower vasopressor therapy (38/168 [22.6%] vs. 66/138 [47.8%], $P < 0.00010$),

Table 1: Characteristics of the study patients

	All patients (*n*=306)	Survivors (*n*=172)	Nonsurvivors (*n*=134)	*P*
Age (years), median (IQR)	63.0 (56.0–72.0)	62.0 (55.0–70.0)	65.00 (58.0–73.0)	0.02
Male sex, *n* (%)	209 (68.3)	111 (64.5)	98 (73.1)	0.11
Female sex, *n* (%)	97 (31.7)	61 (35.5)	36 (26.9)	
BMI (kg/m^2), median (IQR)	24.4 (21.1–29.0)	23.9 (20.1–28.6)	24.9 (21.4–29.4)	0.11
Chronic illnesses, *n* (%)				
Cardiac	65 (21.2)	28 (16.3)	37 (27.6)	0.02
Respiratory	77 (25.2)	39 (22.7)	38 (28.4)	0.26
Renal	19 (6.2)	6 (3.5)	13 (9.7)	0.03
Hepatic	17 (5.6)	5 (2.9)	12 (9.0)	0.02
Diabetes	116 (37.9)	62 (36.0)	54 (40.3)	0.45
Hypertension	141 (46.1)	77 (44.8)	64 (47.8)	0.60
Smoking status, *n* (%)				0.78
Active smoker	38/132 (12.4)	28/95 (16.3)	10/37 (7.5)	0.98
Nonsmoker	64/132 (20.9)	46/95 (26.7)	18/37 (13.4)	0.78
Past smoker	30/132 (9.8)	21/95 (12.2)	9/37 (6.7)	
Missing data 174/306 patients				
Baseline functional status (modified Rankin Scale), *n* (%)				
0-No symptoms	21 (7.1)	11 (6.5)	10 (7.8)	<0.0001
1-No significant disability	73 (24.7)	60 (35.7)	13 (10.2)	
2-Slight disability	67 (22.6)	37 (22.0)	30 (23.4)	
3-Moderate disability	39 (13.2)	17 (10.1)	22 (17.2)	
4-Moderately severe disability	47 (15.9)	19 (11.3)	28 (21.9)	
5-Severe disability	49 (16.6)	24 (14.3)	25 (19.5)	
Missing data in 10/306 patients				
Baseline moderate-to-severe disability, *n* (%)	135 (45.6)	60 (35.7)	75 (58.6)	<0.0001
Histological type of lung cancer, *n* (%)				
NSCLC	239/271 (88.2)	143/157 (91.1)	96/114 (84.2)	
SCLC	26/271 (9.6)	8/157 (5.1)	18/114 (15.8)	0.002
Other cancer histology	6 (2.2)	6/157 (3.8)	0/114 (0)	
Missing in 35/306 patients				
NSCLC type, *n/N* (%)				
Adenocarcinoma	149/193 (77.2)	94/123 (76.4)	55/70 (78.6)	0.36
Large cell	1/193 (0.5)	0/123 (0.0)	1/70 (1.0)	
Squamous cell carcinoma	43/193 (22.3)	29/123 (23.6)	14/70 (20.0)	
Missing data in 78/271 patients with NSCLC				
Cancer stage of NSCLC at the time of diagnosis, *n* (%)				
I	14/135 (10.4)	11/102 (10.8)	3/33 (9.1)	0.64
II	5/135 (3.7)	4/102 (3.9)	1/33 (3.0)	
III	16/135 (11.9)	15/102 (13.7)	2/33 (6.1)	
IV	100/135 (74.1)	75/102 (71.6)	27/33 (81.8)	
Missing data in 104/271 patients with NSCLC				
Cancer stage of NSCLC at the time of ICU admission, *n* (%)				
I	6/200 (3.0)	5/125 4.0)	1/75 (1.3)	0.04
II	4/200 (2.0)	4/125 (3.2)	0/75 (0.0)	
III	19/200 (9.5)	16/125 (12.8)	3/75 (4.0)	
IV	171/200 (85.5)	100/125 (80.0)	71/75 (94.7)	
Missing data in 71/271 patients with NSCLC				
Cancer stage of SCLC at the time of diagnosis, *n* (%)				0.44
Extensive	17/18 (6.5)	7/8 (5.2)	10/10 (8.2)	
Limited	1/18 (0.7)	1/8 (1.2)	0/10 (0.0)	
Missing data in 9/26 patients with SCLC				
Cancer stage of SCLC at the time of ICU admission, *n* (%)				1.0
Extensive	20/20 (100)	8/8 (100)	12/12 (100)	
Limited	0/20 (0)	0/8 (0)	0/12 (0)	
Missing data in 6/26 patients with SCLC				

Contd...

Table 1: Contd...

	All patients (*n*=306)	Survivors (*n*=172)	Nonsurvivors (*n*=134)	*P*
Mutations, *n* (%)				
Any gene mutation/oncogene positive	54/77 (70.1)	42/53 (79.2)	12/24 (50.0)	0.01
EGFR mutation	26/77 (33.8)	24/53 (45.3)	2/24 (8.3)	0.001
KRAS mutation	12/77 (15.6)	8/53 (15.1)	4/24 (16.7)	1.000
ALK positive	8/77 (10.4)	6/53 (11.3)	2/24 (8.3)	1.000
Preadmission treatment, *n* (%)				
Chemotherapy	77/170 (45.3)	53/121 (43.8)	24/49 (49.0)	0.54
Carbo/cisplatin-based chemotherapy	43	28	15	
Immunotherapy	20	14	6	
Radiation	31/170 (18.2)	19/121 (15.7)	12/49 (24.5)	0.18
Surgery for lung cancer	25/170 (14.7)	24/121 (19.8)	1/49 (2.0)	0.003
Missing data about preadmission treatment in 136/306 patients				
Duration between diagnosis and ICU admission (months), median (IQR)	1.0 (0.0, 5.0)	1.0 (0.0, 4.0)	2.0 (0.0, 8.3)	0.58
Admission type, *n* (%)				0.74
Medical	297 (97.1)	166 (96.5)	131 (97.8)	
Surgical	9 (2.9)	6 (3.5)	3 (2.2)	
Admission GCS, median (IQR)	15 (11–15)	15 (15–15)	11 (7–15)	<0.0001
Admission APACHE II, median (IQR)	24.0 (19.0–31.0)	18.0 (15.0–22.3)	27.0 (22.0–33.3)	<0.0001
PO_2:FiO_2 (mm Hg), median (IQR)	153 (86–264)	201 (98–287)	121 (81–200)	0.001
Platelet count (×10^9/L), median (IQR)	285 (167–391)	296 (206–389)	248 (107–409)	0.049
Creatinine (μmol/L), median (IQR)	72.0 (55.0–101.8)	68.0 (54.85–89.3)	77.0 (55.0–130.8)	0.02
Lactate (mmol/L), median (IQR)	1.9 (1.3–3.0)	1.6 (1.2–2.4)	2.4 (1.5–4.1)	<0.0001
INR, median (IQR)	1.1 (1.0–1.3)	1.1 (1.0–1.2)	1.2 (1.1–1.4)	<0.0001
Admission period, *n* (%)				
1999–2005	27 (8.9)	12 (7.1)	15 (11.4)	<0.0001
2006–2010	42 (13.9)	14 (8.2)	28 (21.2)	
2011–2015	69 (22.8)	26 (15.3)	43 (32.6)	
After 2015	164 (54.3)	118 (69.4)	46 (34.8)	

ALK=Anaplastic lymphoma kinase, APACHE=Acute physiology and chronic health evaluation, EGFR=Epidermal growth factor receptor, GCS=Glasgow Coma Scale, ICU=Intensive care unit, IQR=Interquartile range, KRAS=Kirsten rat sarcoma, SCLC=Small cell lung cancer, NSCLC=Non-small lung cancer, PO2:FiO2=The ratio of arterial oxygen partial pressure to fractional inspired oxygen, BMI=Body mass index, INR=International normalized ratio

Table 2: Management of the study patients in the intensive care unit

	All patients (*n*=306)	Survivors (*n*=172)	Nonsurvivors (*n*=134)	*P*
Vasopressor use within 24 hours of admission, *n* (%)	104 (34.0)	26 (15.1)	78 (58.2)	<0.0001
Noninvasive ventilation, *n* (%)	91/170 (53.5)	56/121 (46.3)	35/49 (71.4)	0.003
Missing data in 136/306 patients				
Noninvasive ventilation not followed by intubation, *n* (%)	51/91 (56.0)	40/51 (78.4)	11/51 (21.6)	0.0002
Noninvasive ventilation followed by intubation, *n* (%)	40/91 (44.0)	16/40 (40.0)	24/40 (60.0)	
Intubation and mechanical ventilation, *n* (%)	144 (47.1)	38 (22.1)	106 (79.1)	<0.0001
New renal replacement therapy for acute kidney injury, *n* (%)	27 (8.8)	14 (8.1)	13 (9.7)	0.63
Tracheostomy, *n* (%)	16 (5.2)	5 (2.9)	11 (8.2)	0.04
Do-not-resuscitate order during ICU stay, *n* (%)	92 (30.1)	12 (7.0)	80 (59.7)	<0.0001

ICU=Intensive care unit

invasive mechanical ventilation therapy (51/168 [30.4%] vs. 93/138 [67.4%], $P < 0.00010$), and do-not-resuscitate orders therapy (26/168 [15.5%] vs. 66/138 [47.8%], $P < 0.00010$).

Hospital mortality

In this study, 134/306 patients (43.8%) died in the hospital. Hospital nonsurvivors were older and had a higher prevalence of chronic diseases and more preadmission functional disability than survivors. They also had higher APACHE II scores and more severe abnormalities in laboratory tests on ICU admission (such as higher creatinine and lactate).

Figure 1 describes the mortality of all patients and certain patient groups in four different admission periods (1999–2005, 2006–2010, 2011–2015, and 2016–2020). The mortality rate was lowest in the patients who were admitted after 2015 (28.0%) in the whole cohort compared with 55.6% in the 1999–2005 period, 66.7%

in the 2006–2010 period, and 62.3% in the 2011–2015 period ($P < 0.001$ for between-group difference). Similar mortality patterns in these periods were seen in patients who received mechanical ventilation, had stage IV NSCLC, and had a do-not-resuscitate order [Figure 1]. Of note, most patients (80/92, 87.0%) who had do-not-resuscitate orders while in the ICU died in the hospital.

Stepwise multivariable logistic regression analysis identified the following variables as the independent predictors of hospital mortality [Table 3]: Moderate/severe disability (OR 2.65, 95% 1.22, 5.78), advanced lung cancer (OR 8.36, 95% CI 1.81, 38.58), serum lactate (OR 1.45, 95% 1.12, 1.88), invasive mechanical ventilation (OR 10.92, 95% CI 4.98, 23.95), and admission period after 2015 (OR 0.37, 95% CI 0.16, 0.85).

For the group of patients with known use of noninvasive ventilation (91 patients), death in the hospital occurred in 11 of the 51 (21.6%) who did not require intubation and 24 of the 40 (60.0%) who needed intubation ($P = 0.0002$).

Other outcomes

The outcomes of patients are presented in Table 4. Most of the deaths (105/132 patients, 79.5%) occurred in the ICU. The median duration of mechanical ventilation for the intubated patients was 7.0 days (IQR 2.0, 15.0). The median lengths of stay were 6.0 days (IQR 2.0, 13.0) in the ICU and 14.0 days (IQR 7.0, 26.0) in the hospital and were longer in nonsurvivors than survivors.

Discussion

The main findings of this study were: Most patients with lung cancer admitted to the ICU had advanced cancer with significant preadmission functional disability; life support measures were commonly used in the ICU; the goals of care were changed from full support to limited support (do-not-resuscitate orders) in almost one third of patients; the mortality rate was high but has decreased significantly after 2015; predictors of mortality included older age, poor functional status, vasopressor therapy, and invasive mechanical ventilation.

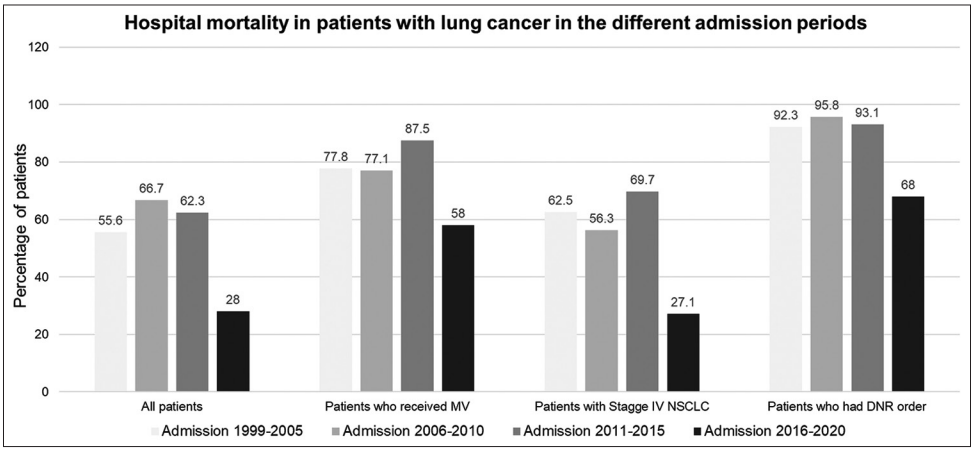

Figure 1: Mortality rates during four different admission periods for all patients ($P < 0.001$), patients who received mechanical ventilation ($P = 0.01$), patients who had stage IV non-small cell lung cancer at admission to the intensive care unit (ICU) (<0.001) and patients who had do-not-resuscitate orders while in the ICU ($P = 0.01$)

Table 3: Predictors of do-not-resuscitate order and of hospital mortality for the study patients (stepwise logistic regression analysis)

	Do-not-resuscitate order			Hospital mortality		
	OR	95% CI	*P*	OR	95% CI	*P*
Age per year increment	NS	NS	-	1.03	1.0–1.06	0.10
Diabetes	2.56	1.15–5.70	0.02	NS	NS	-
Chronic cardiac disease	2.58	1.04–6.39	0.04	2.49	0.99–6.26	0.05
Moderate/severe versus normal/mild functional disability	NS	NS	-	2.65	1.22–5.78	0.01
Advanced lung cancer (stage IV for NSCLC and extensive stage for SCLC) versus less advanced	11.57	1.29–103.7	0.03	8.36	1.81–38.58	0.01
Serum lactate per mmol/L increment	NS	NS	-	1.45	1.12–1.88	0.01
Vasopressor use	0.43	0.17–1,12	0.08			
Invasive mechanical ventilation	9.88	3.83–25.51	<0.0001	10.92	4.98–23.95	<0.0001
Admission period 1999–2015 versus 2016 and after	0.26	0.12–0.59	0.001	0.37	0.16–0.85	0.02

NS=Not significant, SCLC=Small cell lung cancer, NSCLC=Non-small lung cancer, OR=Odds ratio, CI=Confidence interval

Table 4: Outcomes of the study patients

	All patients (*n*=306)	Survivors (*n*=172)	Non-survivors (*n*=134)	*P*
ICU mortality, *n* (%)	105 (34.3)	0	105 (78.4)	<0.0001
MV duration (days) for the patients who were intubated, median (IQR)	7.0 (2.0–15.0)	3.0 (1.0–17.5)	8.0 (3.0–15.0)	0.09
ICU length of stay (days), median (IQR)	6.0 (2.0–13.0)	5.0 (2.0–10.0)	8.5 (3.0–18.0)	<0.0001
Hospital length of stay (days), median (IQR)	14.0 (7.0–26.0)	12.0 (6.0–21.0)	20.00 (9.0–32.0)	0.001
Any venous thromboembolism, *n* (%) Missing data on 136/306 patients	16/170 (9.4)	8/121 (6.6)	8/49 (16.3)	0.08
Pulmonary embolism, *n* (%) Missing data on 136/306 patients	11/170 (6.5)	5/121 (4.1)	6/49 (12.2)	0.08
Deep-vein thrombosis, *n* (%) Missing data on 136/306 patients	11/170 (6.5)	7/121 (5.8)	4/49 (8.2)	0.73

ICU=Intensive care unit, IQR=Interquartile range, MV=Mechanical ventilation

Lung cancer is the most frequent cancer among men and women accounting for 2.09 million cases out of 18 million cancer cases worldwide in 2018.[20] In Saudi Arabia, 852 new cases were diagnosed in 2020 and this number is expected to rise to 1058 in 2030.[21] We studied 306 patients with lung cancer admitted to the adult ICUs of one tertiary-care center in Saudi Arabia. Most of these patients had advanced disease and needed significant organ support, with approximately two-thirds of patients requiring respiratory support, one-third vasopressor therapy, and one-tenth renal replacement therapy. Similar organ support was observed in other studies. In a large cohort of patients with lung cancer (449 patients) from Europe and South America, 53% of the total cohort received ventilatory support and 34% vasopressor therapy.[8,22] Noninvasive ventilation was used in 91/170 patients with available data. Noninvasive ventilation use has been increasing with time due to proven benefits in patients with cancer.[23] Moreover, 30% of patients in the current study had do-not-resuscitate orders placed during their ICU stay after admission. In one cohort study, 31% of patients cohort had do-not-resuscitate orders after a median of 4 days of ICU admission.[8] In another study, almost one-half (49%) of patients transitioned from full support to having a do-not-resuscitate order after a median of 7 days in the ICU.[24] In the current study, 87.0% of the patients who had do-not-resuscitate orders died in the hospital. Similar rate (80%) was observed in other studies.[8]

Intensivists and oncologists play a key role in the end-of-life decision for patients with lung cancer who are admitted to the ICU. Hence, it is important to know the predictors of their mortality. In our study, poor functional status, advanced lung cancer, shock state (higher serum lactate), and acute respiratory failure requiring intubation were the predictors of hospital mortality. Other studies had observed similar findings.[6,10,25-27] Advanced age and male sex were also found to be significant mortality predictors.[9]

In our study, there was a significant decrease in hospital mortality of the study patients admitted to the ICU after 2015 from approximately 60% to 28%. This decrease was noted even in patients with higher mortality risk (stage IV NSCLC and use of invasive mechanical ventilation). The prognosis of patients with solid cancer requiring ICU admission has improved with time.[28] The period after 2015 correlated with the opening of a separate cancer center in our institution with a dedicated ICU and a radiation oncology unit. This was associated with an increased oncology bed capacity, increased referrals of patients with lung cancer, and more availability of novel therapies. The temporal trend of improved survival may have been due to multiple factors. First, the patient mix may have changes after 2015. Second, the implementation of multidisciplinary treatment approaches in the cancer center may have led to more comprehensive and individualized treatment plans from different specialties for patients with cancer. Third, the opening of a dedicated oncology ICU may have led to more standardization of ICU medical and nursing care for those requiring ICU admission. Dedicated oncology ICUs have been shown to improve the processes of care and possibly outcomes.[29,30] The advancement of precision medicine and targeted therapies in the last decade has significantly improved the outcome of lung cancer in specific patient groups.[9] A population-based study in the United States found that the mortality from NSCLC fell sharply from 2013 to 2016, likely due to a reduction in cancer incidence and treatment advances.[31]

The study results should be interpreted in light of its strengths and weaknesses. The retrospective design led to the inability to obtain certain data, especially those that were old. This study only assessed patients admitted to one center in Riyadh, Saudi Arabia. We also performed limited data collection and did not note the use of certain variables such as high-flow nasal oxygen or chemotherapy while in the ICU. Hence, the observed associations could be related to unmeasured confounders. The missingness of data prevented the addition of certain variables in the multivariable logistic

regression analysis (for example, noninvasive ventilation and targeted cancer therapy). On the other hand, the sample size was relatively large, and the study spanned a long period thus allowing a better understanding of the temporal changes in the prognosis of these patients.

Conclusions

Most patients with lung cancer admitted to the ICU had advanced disease and many required different forms of organ support. Their mortality decreased after 2015. Functional disability, advanced lung cancer stage, vasopressor use, and invasive mechanical ventilation predicted mortality. Further multi-centered studies are needed for a better understanding of patients with lung cancer when they develop critical illness.

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Conflicts of interest
There are no conflicts of interest.

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