Selection criteria for intensive care unit referral of lung cancer patients: a pilot study

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ABSTRACT The decision-making process for the intensity of care delivered to patients with lung cancer and organ failure is poorly understood, and does not always involve intensivists. Our objective was to describe the potential suitability for intensive care unit (ICU) referral of lung cancer in-patients with organ failures.

We prospectively included consecutive lung cancer patients with failure of at least one organ admitted to the teaching hospital in Grenoble, France, between December 2010 and October 2012.

Of 140 patients, 121 (86%) were evaluated by an oncologist and 49 (35%) were referred for ICU admission, with subsequent admission for 36 (73%) out of those 49. Factors independently associated with ICU referral were performance status ⩽2 (OR 10.07, 95% CI 3.85–26.32), nonprogressive malignancy (OR 7.00, 95% CI 2.24–21.80), and no explicit refusal of ICU admission by the patient and/or family (OR 7.95, 95% CI 2.39–26.37). Factors independently associated with ICU admission were the initial ward being other than the lung cancer unit (OR 6.02, 95% CI 1.11–32.80) and an available medical ICU bed (OR 8.19, 95% CI 1.48–45.35).

Only one-third of lung cancer patients with organ failures were referred for ICU admission. The decision not to consider ICU admission was often taken by a non-intensivist, with advice from an oncologist rather than an intensivist.

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Introduction

The mortality rate among lung cancer patients admitted to the intensive care unit (ICU) has dropped from 85% in 1986 [1] to 22–47% in 2005 [2–6]. These survival gains are ascribable to improvements in anticancer drugs [7–9] and intensive care [10], as well as to changes in criteria for ICU admission [11]. Selection of the intensity of care delivered to lung cancer patients with organ failure is based on the medical history [2–6], opinion of the oncologist and intensivist, and wishes of the patient and family. Available studies are retrospective [2–6] or confined to patients referred for ICU admission [12]. No published study has investigated the criteria for ICU referral of lung cancer patients or the impact of ICU referral and admission on patient outcomes.

Our objective here was to describe the potential suitability for ICU referral of lung cancer in-patients. We conducted a prospective, observational cohort study of lung cancer in-patients with organ failure.

Materials and methods

Study design and patients

We included all patients with lung cancer and failure of at least one organ admitted to any of the departments of the teaching hospital in Grenoble, France, between December 1, 2010, and October 31, 2012. Organ failure development during the postoperative period was an exclusion criterion.

Our primary objective was to identify factors associated with referral for ICU admission. The secondary objectives were to identify factors associated with ICU admission and to evaluate the consequences of intensity of care on patient outcomes, namely, mortality, psychological distress and hospital experience. This study was registered at www.ClinicalTrials.gov with the identifier NCT00222404.

The definition of organ failure used for the study is provided in online supplementary table S1. The appropriateness of ICU admission was discussed with the thoracic oncologist in charge of the patient, if available, and with the intensivist if contacted by the first physician in charge of the patient. Intensity of care decisions were based on the patient's performance status, lung cancer characteristics and organ failure, and the wishes of the patient and family, particularly regarding ICU admission. The reasons for choosing the initial intensity of care were recorded. Patients were followed prospectively in their hospital department. After 3 months, patients without cognitive disorders or terminal palliative care underwent an interview with a psychologist to evaluate their experience during their acute illness.

Data collection

The following data were collected prospectively: histological type of cancer, cancer status (remission, newly diagnosed or progression/recurrence), cancer spread (TNM classification 13), anticancer treatment, performance status (Eastern Cooperative Oncology Group Performance Status (ECOG-PS) 14) and Logistic Organ Dysfunction score to evaluate the acute disease. Prospective data on the circumstances of the decision-making process for determining ICU referral were as follows: hospital department, decision made during the day or off-hours, advice from specialists if any, number of beds available in the medical ICU at the time of organ failure development and reason for ICU admission refusal where relevant.

After 3 months, we recorded the ECOG-PS and the patients were assessed using the Hospital Anxiety and Depression Scale (HADS) [15], with sub-score cut-offs $\geqslant$11 defining anxiety disorders or depression; the revised Impact of Event Scale (IES-R), with a total score >25 defining moderate-to-severe post-traumatic stress disorder (PTSD) [16, 17]; and the 36-item Short Form (SF-36), with higher scores on the Physical Component Summary (PCS) and Mental Component Summary (MCS) subscales indicating better health-related quality of life. These instruments were completed in the presence of a psychologist, both to alleviate patient anxiety related to the evaluation and to ensure that the patients fully understood all items.

Statistical analysis

Continuous variables are presented as median (interquartile range (IQR)) and categorical variables as n (%). Associations between categorical variables were compared using the Chi-squared test or Fisher's exact test and those between continuous variables using the Wilcoxon test. No patient was lost to follow-up. Patients were followed until April 1, 2014.

To identify associations between patient characteristics and referral for ICU admission, ICU admission or 3-month mortality, we built univariate logistic regression models and computed the odds ratios with their 95% confidence intervals. A preliminary choice between collinear variables was performed based on clinical relevance, accuracy of data entry and the Akaike Information Criterion [18]. Variables with $p<0.20$ were proposed to a stepwise procedure and were kept in the multiple logistic regression models when they yielded p-values $\leqslant$0.05 in the multivariate context.

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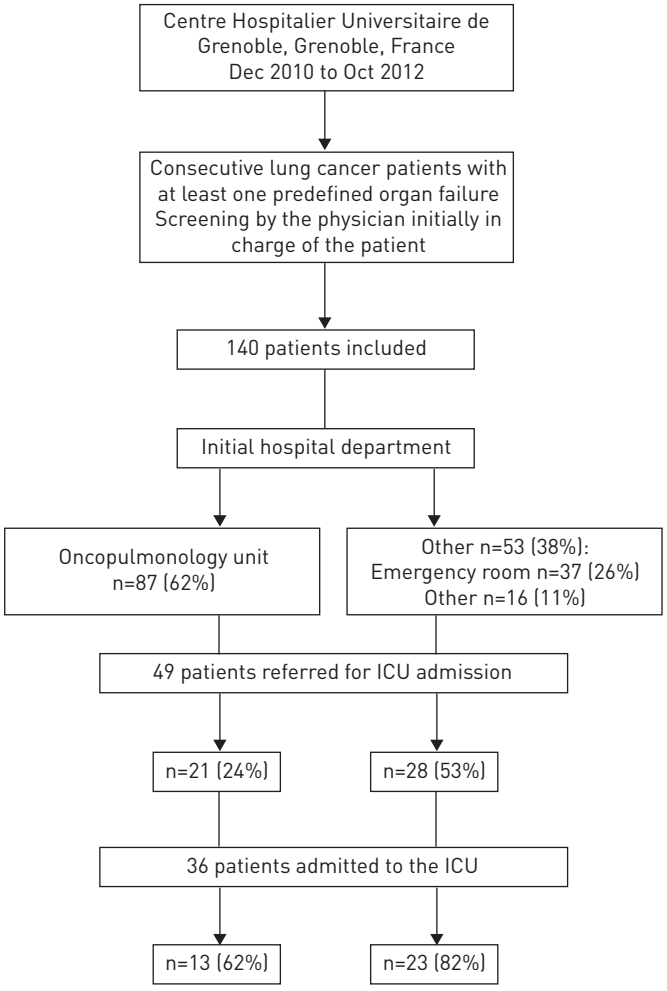

FIGURE 1 Flow chart. ICU: intensive care unit.

Kaplan–Meier plots of survival curves from organ failure onset were compared between groups using the log-rank test. The aforementioned method was used to select variables for a multivariate Cox model.

All tests were two-sided and p-values <0.05 were considered statistically significant. All statistical analyses were performed using SAS 9.3 (SAS Institute, Cary, NC, USA).

Results

Patient characteristics

We included 140 patients (fig. 1). During the study period, 550 patients were admitted to the emergency room and 1532 to other hospital departments for reasons other than cancer surgery. Table 1 lists the main patient characteristics and table 2 the characteristics of their critical illnesses. Among patients who developed organ failure, 82 (62%) were referred from the lung cancer unit, 37 (26%) from the emergency room and 16 (11%) from other hospital departments.

Patient characteristics according to their initial department of admission are reported in table S2. Patients who developed organ failure in the lung cancer unit more often had an ECOG-PS >2 (OR 3.70, 95% CI 1.80–7.61) than did patients who developed organ failure in other hospital departments. Patients in the lung cancer unit had a longer median time from cancer diagnosis to organ failure (median 7.1 months (IQR 1.5–20.7 months) *versus* 2.3 months (IQR 0.5–8.8 months), p=0.01) and more often had progressive disease (OR 2.50, 95% CI 1.18–5.32).

Of the 140 patients, 54 (39%) said that they would agree to ICU admission should this option be offered to them and 49 (35%) that they would refuse ICU admission; for the remaining 37 (26%) patients, no information on patient wishes was available, and 20 (54%) out of these 37 patients were not competent at the time they developed organ failure. Advice from the oncologist was obtained for 121 (86%) patients and 49 (35%) patients were referred for ICU admission, including 36 (73%) out of 49 who were admitted to the ICU.

TABLE 1 Patient characteristics according to referral for intensive care unit (ICU) admission

	All patients	Not referred for ICU admission	Referred for ICU admission	p-value
Patients	140	91 (65)	49 (35)	
Demographics				
Sex				0.57
Male	104 (74)	69 (66)	35 (34)	
Female		22 (61)	14 (39)	
Age years	65 (58–74)	64 (58–74)	67 (59–72)	0.84
Performance status				$<10^{-4}$
0–2	55 (39)	20 (26)	35 (64)	
3–4	85 (61)	71 (84)	14 (16)	
Modified CCI				0.84
0	93 (66)	61 (66)	32 (34)	
⩾1	47 (34)	30 (64)	17 (36)	
Weight loss %	11 (7–20)	13 (7–20)	9 (6–17)	0.08
Cancer history				
Time from cancer diagnosis months	5.0 (1.0–15.4)	6.3 (1.5–17.4)	1.8 (0.7–8.8)	0.01
Type of cancer				0.10
Adenocarcinoma	66 (47)	45 (68)	21 (32)	
Squamous cell carcinoma	23 (16)	10 (43)	13 (57)	
Small cell carcinoma	26 (19)	17 (65)	9 (35)	
Other	25 (18)	19 (76)	6 (24)	
Metastasis at inclusion				10^{-3}
Yes	119 (85)	84 (71)	35 (29)	
No	21 (15)	7 (33)	14 (67)	
Cancer status				$<10^{-4}$
Controlled disease	18 (13)	8 (44)	10 (56)	
Progression	52 (37)	46 (88)	6 (12)	
Unknown	36 (26)	21 (58)	15 (42)	
Not yet treated	34 (24)	16 (47)	18 (53)	
Current anticancer treatment				$<10^{-4}$
None	48 (34)	46 (96)	2 (4)	
Awaiting treatment	40 (29)	19 (48)	21 (53)	
Treatment ongoing	45 (32)	24 (53)	21 (47)	
Therapeutic window	7 (5)	2 (29)	5 (71)	
Patient/family stated they refuse ICU admission				$<10^{-4}$
Yes	49 (35)	44 (90)	5 (10)	
No	91 (65)	47 (52)	44 (48)	

Data are presented as n, n (%) or median (interquartile range), unless otherwise stated. CCI: Charlson Comorbidity Index [19].

Of the eight patients for whom no bed was available in the hospital's medical ICU, seven were admitted to ICUs in other hospitals or to the same hospital's intermediate care unit; the remaining patient stayed in the emergency room.

Intensity of care was ICU admission in 36 (26%) patients, maximal medical care without ICU admission in 52 (37%) patients and palliative care in 52 (37%) patients.

Referral for ICU admission

The main reason for not referring patients for ICU admission (n=91, 65%) was refusal by the patient and/or family (n=44, 48%). The other main reasons given by the non-intensivists initially in charge of the patient (with several reasons per patient in some cases) were a decision to provide palliative care (n=31, 34%), a bedridden patient (n=27, 30%), at least three different lines of chemotherapy (n=16, 18%), active brain metastasis (n=15, 16%) and highly aggressive cancer (n=11, 12%).

The univariate analysis results are reported in tables 1 and 2. Referral for ICU admission was more common when the physician in charge was not a lung cancer specialist ($p=6\times10^{-4}$). Factors independently associated with referral for ICU admission were ECOG-PS ⩽2 (OR 10.07, 95% CI 3.85–26.32), nonprogressive malignancy (OR 7.00, 95% CI 2.24–21.80), and absence of refusal stated explicitly by the patient and/or family (OR 7.95, 95% CI 2.39–26.37).

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TABLE 2 Characteristics of the acute illnesses according to referral for intensive care unit (ICU) admission

	All patients	Not referred for ICU admission	Referred for ICU admission	p-value
Patients	140	91 (65)	49 (35)	
Setting of organ failure development				
Initial department				6×10^{-4}
Pulmonology unit	87 (62)	66 (76)	21 (24)	
Emergency or other ward	53 (38)	25 (47)	28 (53)	
Time of organ failure				0.06
Standard working hours	107 (76)	74 (69)	33 (31)	
Off-hours	33 (24)	17 (52)	16 (48)	
Time from hospital admission to organ failure days	3 (0–11)	5 (0–14)	1 (0–5)	2×10^{-3}
Acute disease				
Organ(s) involved				
Neurological				
Yes	67 (48)	52 (78)	15 (22)	3×10^{-3}
No	73 (52)	39 (53)	34 (47)	
Respiratory				
Yes	64 (46)	33 (52)	31 (48)	2×10^{-3}
No	76 (54)	58 (76)	18 (24)	
Cardiovascular				
Yes	36 (26)	16 (44)	20 (56)	3×10^{-3}
No	104 (74)	75 (72)	29 (28)	
Renal				
Yes	10 (7)	6 (60)	4 (40)	0.74
No	130 (93)	85 (65)	45 (35)	
Hepatic				
Yes	6 (4)	5 (83)	1 (17)	0.67
No	134 (96)	86 (64)	48 (36)	
LOD score	1 (1–2)	1 (1–1)	2 (1–7)	$<10^{-4}$

Data are presented as n, n (%) or median (interquartile range), unless otherwise stated. LOD: Logistic Organ Dysfunction.

ICU admission

Tables 3 and 4 report the characteristics of the patients referred for ICU admission according to whether they were admitted. The main reasons for not admitting a patient (n=13) given by the intensivists were excessive tumour spread (six (46%) out of 13 patients) and excessive severity of the acute illness (five (38%) out of 13). Among patients admitted to the ICU, 21 received vasopressors, 21 invasive mechanical ventilation and seven noninvasive ventilation.

In the patients referred for ICU admission, none of the demographic variables or critical-illness characteristics was significantly associated with ICU admission by univariate analysis. ICU admission decisions were similar during working days and during nights and weekends. By multivariate analysis, factors associated with ICU admission were initial admission to a department other than the lung cancer unit (OR 6.02, 95% CI 1.11–32.80) and an available bed in the hospital's medical ICU (OR 8.19, 95% CI 1.48–45.35).

After initial refusal, two patients were subsequently admitted to the ICU but died during the ICU stay.

Survival rates and prognostic factors

Among patients initially admitted to the ICU, 18 (50%) died in the ICU, and six others died between ICU discharge and hospital discharge. In-hospital mortality was 63% (n=33) among patients who received maximal medical care without ICU admission and 94% (n=49) among those who received palliative care. In the overall population, median survival was 5 days (IQR 1–26 days, range 0–981 days). Figure 2 shows survival according to referral for ICU admission and to ICU admission. Table 5 reports the results of the univariate analysis. Independent predictors of death were poor chronic health status, neurological or respiratory failure, and refusal of ICU admission by the patient or relatives. Interestingly, by multivariate analysis (table 5), ICU admission was not associated with survival. Only performance status was independently associated with 3-month survival (data not shown).

Among hospital survivors (n=34, 24%), median survival after hospital discharge was 337 days (IQR 58–711 days) in patients admitted to the ICU (n=12), 58 days (IQR 9–118 days) in those who received maximal medical care (n=19) and 29 days (IQR 12–349 days) in those who received palliative care (n=3).

TABLE 3 Characteristics of patients referred for intensive care unit (ICU) admission according to whether they were admitted

	Admitted to the ICU	Not admitted to the ICU	p-value
Patients	36 (73)	13 (27)	
Demographics			
Sex			0.73
Male	25 (71)	10 (29)	
Female	11 (79)	3 (21)	
Age years	67 (59–74)	64 (57–70)	0.46
Performance status			0.48
0–2	27 (77)	8 (23)	
3–4	9 (64)	5 (36)	
Modified CCI			0.50
0	22 (69)	10 (32)	
⩾1	14 (82)	3 (18)	
Weight loss %	10 (4–17)	9 (6–13)	0.54
Cancer history			
Time from cancer diagnosis	1 (0–6)	9 (1–19)	0.11
Type of cancer			0.30
Adenocarcinoma	18 (86)	3 (14)	
Squamous cell carcinoma	9 (69)	4 (31)	
Small cell carcinoma	5 (56)	4 (44)	
Other	4 (67)	2 (33)	
Metastasis at inclusion			0.30
Yes	24 (69)	11 (31)	
No	12 (86)	2 (14)	
Cancer status			0.65
Controlled disease	7 (70)	3 (30)	
Progression	4 (67)	2 (33)	
Unknown	10 (67)	5 (33)	
Not yet treated	15 (83)	3 (17)	
Current anticancer treatment			0.65
None	1 (50)	1 (50)	
Awaiting treatment	17 (81)	4 (19)	
Treatment ongoing	14 (67)	7 (33)	
Therapeutic window	4 (80)	1 (20)	
Patient/family explicitly refused ICU admission			0.60
Yes	3 (60)	2 (40)	
No	33 (75)	11 (25)	

Data are presented as n (%) or median (interquartile range), unless otherwise stated. CCI: Charlson Comorbidity Index [19].

Only two patients with ECOG-PS >2 at baseline were still alive after 3 months. Both had progressive malignancies and neither was admitted to the ICU. After 3 months, their ECOG-PS was 4 and they were in palliative care without having received further anticancer treatment.

Evaluation at 3 months

At 3 months, only 19 (14%) patients were still alive, including 10 who underwent a psychological evaluation; one of these patients was not assessed using the HADS, IES-R of SF-36. The reasons for not undergoing this evaluation in the other nine patients were end-of-life (EOL) setting (n=3), cognitive disorders (n=3), patient refusal (n=2) and loss to follow-up (n=1).

HADS results showed anxiety in one patient and depression in another; both patients had been admitted to the ICU. IES-R results indicated PTSD in five patients; the four patients without PTSD had no anxiety or depression. All 10 evaluated patients had suffered a threatening experience at the psychological and physical levels, and had difficulty coping with the loss of their previous healthy condition. They overinvested their daily activities, which were often limited by physical exhaustion. The mean±SD SF-36 results showed better mental quality of life (MCS 51.2±9.4) than physical quality of life (PCS 35.0±10.4).

Discussion

We report the results of a 2-year, prospective, hospital-wide study designed to evaluate the potential suitability for ICU referral of 140 consecutive patients with lung cancer and failure of one or more organs.

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TABLE 4 Characteristics of acute illnesses in patients referred for intensive care unit (ICU) admission according to whether they were admitted

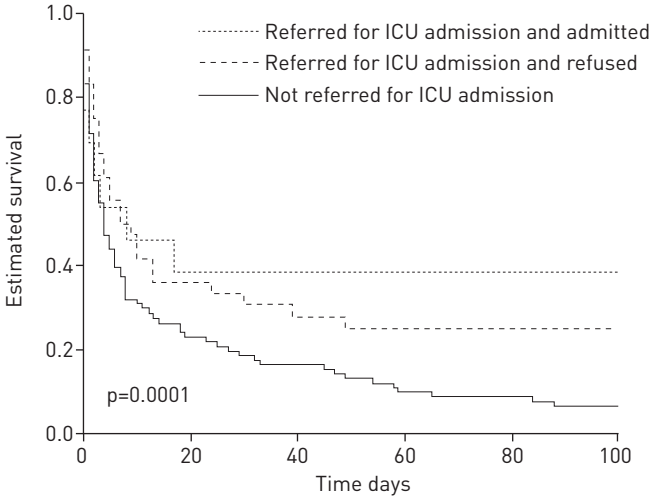
	Admitted to the ICU	Not admitted to the ICU	p-value
Patients	36 (73)	13 (27)	
Setting of organ failure development			
Initial department			0.11
Pulmonology unit	13 (62)	8 (38)	
Emergency or other ward	23 (82)	5 (18)	
Time of organ failure			0.17
Standard working hours	22 (67)	11 (33)	
Off-hours	14 (88)	2 (13)	
Time from hospital admission to organ failure days	0 (0–4)	4 (0–11)	0.18
Bed available in the medical ICU			0.08
No	8 (53)	7 (47)	
Yes	28 (82)	6 (18)	
Acute disease			
Organ(s) involved			
Neurological			
Yes	10 (67)	5 (33)	0.50
No	26 (76)	8 (24)	
Respiratory			
Yes	25 (81)	6 (19)	0.18
No	11 (61)	7 (39)	
Cardiovascular			
Yes	17 (85)	3 (15)	0.13
No	19 (66)	10 (34)	
Renal			
Yes	2 (50)	2 (50)	0.28
No	34 (76)	11 (24)	
Hepatic			
Yes	1 (100)	0 (0)	1
No	35 (73)	13 (27)	
LOD score	2 (1–7)	1 (1–2)	0.11

Data are presented as n (%) or median (interquartile range), unless otherwise stated. If no bed was available in the hospital's medical ICU, patients could be admitted to another ICU or to an intermediate-care unit. LOD: Logistic Organ Dysfunction.

We found that 65% of patients were not referred to the ICU, *i.e.* that intensive care was often withheld by physicians who were not intensivists. Patient-related factors associated with absence of referral for ICU admission were poor ECOG-PS, progressive malignancy, and explicit refusal of ICU admission by the patient and/or family; structure-related factors were initial admission to the lung cancer unit and lack of available beds in the medical ICU.

Strengths of our study include the prospective design and the evaluation of the strategy chosen by the first physician in charge of the patient. A single previous prospective study [12] focused on the decision-making process for ICU admission but this study was confined to patients referred to the ICU and therefore missed the patients for whom the oncologists decided that ICU admission was not appropriate. We also evaluated psychological distress using both standard scales and a psychologist's evaluation in 3-month survivors. The single-centre patient recruitment limits the external applicability of our results. Furthermore, the process of care was probably organised toward cancer patients, as considerable efforts have been made in our institution over the years to improve communication between intensivists and lung cancer specialists regarding the early evaluation and triage of patients. We did not record the details of the discussions regarding treatment-limitation decisions.

Importantly, in our hospital, only 35% of lung cancer patients with organ failure were referred for ICU admission overall, and this proportion was only 24% among patients in the lung cancer unit. Thus, lung cancer specialists had a strong tendency to consider that ICU admission was inappropriate. The main reasons were poor general status of the patient or advanced cancer; another reason identified in nearly half the cases was explicit refusal of ICU admission by the patient and/or family. In a study of 1231 patients with stage IV lung or colorectal cancer [20], 47% of patients received at least one aggressive therapeutic intervention within 30 days before death, including ICU admission (6% of patients), and patient- and surrogate-reported EOL discussions were significantly associated with EOL care. These data emphasise the importance of holding EOL



Time days	0	5	10	20	40	60	80	100
At risk n	140	73	53	40	29	29	21	19
Referred and admitted	36	23	18	14	10	10	9	9
Referred and refused	13	7	6	5	4	4	4	4
Not referred	91	43	29	21	15	9	8	6

FIGURE 2 Kaplan–Meier survival estimate according to referral for intensive care unit (ICU) admission.

discussions attended by physicians and patients. The reasons given for not referring patients to the ICU were straightforward. The main issue is whether intensive care would have improved survival and quality of life had the oncologists (and patients/relatives) been in favour of ICU admission.

Among patients referred for ICU admission, factors associated with ICU admission were initial admission to a department other than the lung cancer unit and an available bed in the medical ICU. In another study [12], among patients with haematological or solid malignancies referred for ICU admission, remission of the malignancy was associated with ICU admission, whereas poor chronic health status and solid malignancy were associated with refusal of ICU admission. In our study, these factors were associated with referral for ICU admission but were not significantly associated with ICU admission among referred patients.

TABLE 5 Univariate and multivariate analyses of factors associated with mortality

Factor	Univariate analysis		Multivariate analysis	
	HR (95%CI)	p-value	HR (95%CI)	p-value
Demographic features				
Age ⩾65 years	1.36 (0.97–1.91)	0.08		
Male sex	1.28 (0.87–1.89)	0.21		
ECOG-PS >2	2.40 (1.63–3.55)	$<10^{-4}$	2.37 (1.56–3.60)	$<10^{-4}$
Modified CCI ⩾0	1.21 (0.85–1.72)	0.30		
Cancer history				
Metastasis at inclusion	1.88 (1.11–3.18)	0.02		
Progression	1.49 (1.04–2.14)	0.03		
Cancer diagnosis >5 months earlier	1.04 (0.74–1.45)	0.82		
Organ failure				
Neurological	1.67 (1.17–2.37)	4×10^{-3}	1.67 (1.12–2.48)	0.01
Respiratory	1.43 (1.02–2.01)	0.04	2.35 (1.60–3.46)	$<10^{-4}$
Cardiovascular	0.82 (0.56–1.22)	0.33		
ICU refusal from patient/relatives	1.66 (1.16–2.38)	4×10^{-3}	1.67 (1.14–2.44)	8×10^{-3}
Referred by pulmonologist	1.61 (1.13–2.30)	8×10^{-3}		
ICU admission	0.61 (0.41–0.91)	0.02		

HR: hazard ratio; ECOG-PS: Eastern Cooperative Oncology Group Performance Status; CCI: Charlson Comorbidity Index [19]; ICU: intensive care unit.

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In keeping with previous studies, factors associated with decreased survival were a poor ECOG-PS [5, 21–24] and respiratory failure [4, 25, 26]. Survival was very poor, in part due to the absence of anticancer treatment in one-third of patients. In patients not receiving anticancer treatment, the development of organ failure can indicate the beginning of the dying process. Survival of patients admitted to the ICU was worse than in previous studies [2, 3, 5], whereas survival was good in patients discharged alive from the hospital, most notably after ICU admission.

All 10 patients evaluated by the psychologist reacted negatively to the stress associated with the acute event. The traumatic effect may have been related to the experience of impending death, although the acute event did not induce psychological trauma. Finally, the traumatic event was described by the patients as a reminder of the severity of the cancer and of the risks related to cancer progression and treatment. This last point constitutes a strong incentive to develop early supportive care and psychological support for cancer patients.

Conclusions

The prognosis of lung cancer with organ failure was very poor, particularly in patients whose ECOG-PS was >2. When organ failure developed, only 35% of patients with lung cancer were referred for ICU admission in our teaching hospital. Thus, the triage decision was often made without advice from intensivists. These results require confirmation by a multicentre study.

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