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UNIVERSITE JOSEPH FOURIER
FACULTE DE MEDECINE DE GRENOBLE

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PRISE EN CHARGE EN REANIMATION DE PATIENTS PORTEURS D'UN CANCER BRONCHIQUE NON RESECABLE

THESE PRESENTEE POUR L'OBTENTION DU DOCTORAT EN MEDECINE

DIPLOME D'ETAT

Anne-Claire TOFFART

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THESE SOUTENUE PUBLIQUEMENT A LA FACULTE DE MEDECINE DE GRENOBLE

Le 16 juin 2010

DEVANT LE JURY COMPOSE DE

Président du jury : Monsieur le Professeur Denis MORO-SIBILOT

Membres du jury : Monsieur le Professeur Jean-François TIMSIT, directeur de thèse

Monsieur le Professeur Christian BRAMBILLA

Madame le Docteur Rébecca HAMIDFAR-ROY

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Résumé

RESUME

Contexte: L'admission des patients porteurs d'un cancer broncho-pulmonaire (CBP) non opérable en réanimation a été longtemps considérée comme déraisonnable. Le but de ce travail est d'étudier le pronostic des patients néanmoins admis. Les facteurs associés à la survie ont été identifiés.

Méthodes: Etude rétrospective de patients porteurs d'un CBP non résécable admis consécutivement dans trois services de réanimation en France (2000-2007, 2005-2007, et 2005-2006, respectivement).

Resultats: Nous avons inclus 103 patients avec un IGS médian [Q1-Q3] de 33 [25-46] et un LOD score médian de 3 [1-4]. Le recours à la ventilation mécanique invasive a été nécessaire pour 41 (40%) patients. Soixante trois (61%) patients étaient métastatiques et 26 (25%) avaient un ECOG performance status (PS) >2. Le motif d'admission en réanimation était une détresse respiratoire aiguë pour 58 (56%) patients. Le taux de survie à 3 mois était de 37% (intervalle de confiance à 95% [IC 95%], 28-46). En analyse multivariée, les variables associées à la mortalité étaient un ECOG-PS >2 (hazard ratio [HR], 2.65; IC 95%, 1.43-4.88), l'existence de métastases à l'admission (HR, 1.90; IC 95%, 1.08-3.33), et un LOD score élevé (HR, 1.19; IC 95%, 1.08-1.32). La décroissance du LOD score au cours des 72 premières heures était corrélée à la survie.

Conclusions: La survie des patients porteurs d'un CBP non résécable admis en réanimation était de 37% après 90 jours. Nos résultats apportent un argument supplémentaire pour une réanimation d'attente chez les patients porteurs d'un CBP non résécable avec des dysfonctions d'organes. La non amélioration après 3 jours de réanimation intensive diminue franchement l'espoir de survie.

Abréviations

ABBREVIATIONS:

AIC: Akaike Information Criterion

APACHE II: Acute Physiology And Chronic Health Evolution II

CCI: Charlson Co-morbidity Index

CI: Confidence Interval

ECOG: Eastern Cooperative Oncology Group

HR: Hazard Ratio

ICU: Intensive Care Unit

IQR: InterQuartile Range

LOD score: Logistic Dysfunction score

MV: Mechanical Ventilation

PS: Performance Status

SAPS II: Simplified Acute Physiology Score II

Article

Use of Intensive Care in Patients with Nonresectable Lung Cancer

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ABSTRACT

Background: Admission of lung cancer patients to the intensive care unit (ICU) has been criticized. We evaluated whether ICU admission improved 3-month survival in patients with nonresectable lung cancer. Factors associated with survival were identified.

Methods: Retrospective study in consecutive non-surgical lung cancer patients admitted to three ICUs in France (2000-2007, 2005-2007, and 2005-2006, respectively).

Results: We included 103 patients with a median [Q1-Q3] SAPS II of 33 [25-46] and a median LOD of 3 [1-4]. Invasive mechanical ventilation was required in 41 (40%) patients. Sixty-three (61%) patients had metastasis and 26 (25%) an ECOG performance status (PS) >2. The reason for ICU admission was acute respiratory failure in 58 (56%) patients. Three-month survival rate was 37% (95% confidence interval [95% CI], 28-46). By multivariate analysis, variables associated with mortality were ECOG-PS >2 (hazard ratio [HR], 2.65; 95% CI, 1.43-4.88), metastasis at admission (HR, 1.90; 95% CI, 1.08-3.33), and worse LOD score (HR, 1.19; 95% CI, 1.08-1.32). The LOD score decrease over the first 72 hours was associated with survival.

Conclusions: Survival in patients with non-surgical lung cancer requiring ICU admission was 37% after 90 days. Our results provide additional evidence that ICU management may be appropriate in patients with nonresectable lung cancer and organ failures.

INTRODUCTION

In 2009, the number of new lung cancer cases in the United States was estimated at 219,440, representing 15% of all new cases of cancer. The same year, lung cancer was responsible for 159,390 deaths (28% of all cancer deaths) and was the most common cause of death from cancer.[1]

Recent therapeutic advances have improved survival in patients with lung cancer including those who are not eligible for surgical treatment.[2,3] Complications related to the cancer itself or to the treatment may result in acute life-threatening events. ICU admission of patients with nonresectable lung cancer has been criticized based on the high mortality rate in this population.[4] The overall 5-year survival rate in patients who are not treated surgically is only 16%.[1] However, advances in pharmacological treatments[2] for lung cancer may have made ICU admission legitimate in situations where life-supporting treatment was previously considered futile.[5] Furthermore, outcomes in cancer patients admitted to the ICU have improved in recent years,[6] as a result of early-admission strategies and new noninvasive diagnostic and therapeutic tools.

ICU management is burdensome, costly, and associated with risks to the patient.[7] ICU admission decisions should be based on short-term and long-term survival data and on patients' wishes and expected post-ICU quality of life.

The objective of this study was to assess ICU, hospital, 90-day, and 1-year survival in lung cancer patients admitted to the ICU. We also sought to identify the effect of LOD score changes over the first 72 hours in the ICU.

METHODS AND MATERIALS

Study Design

We conducted a retrospective review of the medical charts of lung cancer patients admitted to three ICUs in France, in tertiary-level hospitals managing large numbers of cancer patients. In these three ICUs, cancer patients are admitted only if they are eligible for potentially lifespan-extending anti-cancer treatment. The study was approved by the appropriate ethics committee (*Comité d'éthique des Centres d'Investigation Clinique de l'inter-région Rhône-Alpes-Auvergne*), which waived the need for informed consent. The study was retrospective and therefore had no impact on patient management.

Study subjects

Cases were identified through the hospital databases. The case-ascertainment periods in the three ICUs were 2000-2007, 2005-2007, and 2005-2006." During each period, all ICU patients with a past or present history of lung cancer were included. We did not include patients admitted for postoperative management. We reviewed the medical chart of each included patient.

The data in Tables 1 and 2 were abstracted from the medical records. We used the Charlson co-morbidity index (CCI) without the malignant solid tumor item. We recorded the histological type of cancer, cancer status (remission, newly diagnosed, or progression/recurrence), cancer spread (TNM classification[8]), anticancer treatment, and performance status (Eastern Cooperative Oncology Group scale, ECOG-PS[9]). We also recorded the treatments used in the ICU (vasoactive drugs, endotracheal and noninvasive mechanical ventilation (MV), and renal replacement therapy) and the acute organ failures that developed within the first 48 hours in the ICU. The SAPS II severity score and the LOD score were calculated on the first ICU day. Individual organ failure was defined as an LOD score ≥1

point for the relevant organ system. The LOD score and number of organ failures after 48 hours in the ICU were recorded. In August 2008, vital status was assessed based on death registry data. At this time point, 11 patients were lost to follow-up, after a mean of 143 days since hospital discharge.

Statistical Analysis

Continuous variables are reported as median (25% to 75% interquartile range, IQR) and categorical variables as number (percentage). The SAPS II and the LOD score are expressed in points. Survival curves were obtained using the Kaplan-Meier method and compared using the log-rank test. Data for patients who were lost to follow-up were considered censored. Cut points for severity scores were decided prior to the analysis based on clinical discussion and previous work. Univariate and multivariate analyses were used to identify factors associated with 90-day survival. Only variables available on the day of ICU admission were entered into a forward multivariate Cox model stratified by centre. At the first step of variable selection, either the SAPS II or the LOD score was entered. The accuracy of the two non-nested models was compared using the Akaike Information Criterion (AIC).[10] The best model was defined as the model with the lower AIC value. Results were expressed as hazard ratios (HRs), with their 95% confidence intervals (95% CIs) and *P* values. For continuous variables (SAPS II), the assumption of linearity was checked using a categorization approach and the HR was indexed to an increment of one unit. Categorical variables were recorded as absent or present.

RESULTS

Patient Characteristics

We included 105 patients. Only 2 patients were excluded due to missing data. Table 1 reports the main characteristics of the remaining 103 patients. Median follow-up in survivors was 109 (33-227) days. At 3 months, 7 (7%) patients were lost to follow-up.

At referral for ICU admission, 32 (31%) patients were in the emergency room, 8 (8) were being transported to the hospital from home by an emergency mobile unit, and 63 (61%) were on the wards. Most of the patients had squamous-cell carcinoma or adenocarcinoma, which was usually not resectable. In general, the patients had few co-morbidities (median modified CCI, 1 (0-2)) and a good performance status (ECOG-PS ≤2 in 75% of patients). The main reasons for ICU admission are displayed in Table 2.

ICU mortality was 31% and in-hospital mortality was 48%. The Kaplan-Meier estimates of 90-day and 1-year survival rates were 37% (95% CI, 28-46) and 12% (95% CI, 6-18), respectively, with no differences among the three centers. Among the 71 (69%) patients discharged alive from the ICU, median survival after ICU discharge was 104 days (18-227), estimated 90-day survival was 54% (95% CI, 48-60%], and estimated 1-year survival was 18% (95% CI, 13-23%).

The univariate analysis results are reported in Table 3. Mortality after 90 days was not associated with center, age, CCI, time since cancer diagnosis, reason for ICU admission, use of noninvasive MV, or ICU stay length. Variables whose values differed significantly between patients alive and dead after 90 days were ECOG-PS>2, metastatic disease at ICU admission, need for invasive ventilation or vasoactive drugs within 72 hours after ICU admission, and worse severity score (LOD score or SAPS II). Three-month survival was similar in patients who required non-invasive MV (40%) and in those who required no ventilatory assistance (47%) (P=0.71) but was significantly lower in patients who required

endotracheal MV (22%) (*P*=0.02). The multivariate analysis is reported in Table 3. With SAPS II in the model, two variables were associated with 90-day mortality: high SAPS II and ECOG-PS>2. With the LOD score in the model, three variables were associated with 90-day mortality: high LOD score, presence of metastatic disease, and ECOG-PS>2. This last model had a lower AIC value and was therefore selected (Table 3). Kaplan-Meier survival curves comparing low and high ECOG-PS and LOD score values are shown in figure 1.

During the study period, the Kaplan-Meier estimates of 90-day and 1-year survival rates in all lung cancer patients managed at the Albert Michallon Teaching Hospital were 90% (95% CI, 87-92) and 68% (95% CI, 63-72), respectively. In patients with stage I to IIIa lung cancer, these proportions were 96% (95% CI, 93-98) and 85% (95% CI, 79-89), respectively. In patients with extensive disease, they were 82% (95% CI, 76-87) and 44% (95% CI, 37-52), respectively. Thus, the occurrence of a critical illness leading to ICU admission was associated with a considerable decrease in survival.

Impact of organ dysfunctions at 72 hours

Of the 21 (201%) patients with LOD scores higher than 6 after 72 hours, 18 (86%) died in the ICU (figure 2). The other 3 (14%) patients had septic or cardiogenic shock that required renal replacement therapy (5 points in the LOD score). Of the 12 (12%) patients whose LOD score decreased during the first 72 hours, only 1 (8%) died in the ICU. Of the 58 (57%) patients whose LOD score remained unchanged during the first 72 hours, 17 (29%) died. Of the 31 (31%) patients whose LOD score increased during the first 72 hours, 14 (45%) died (*P*=0.06).

Impact of treatment-limitation decisions

All but 7 (7%) patients were admitted to the ICU for unrestricted management. A decision to withhold and/or withdraw life-sustaining treatment was implemented in 13 (13%) additional patients on day 3. These 13 patients died before hospital discharge. In all these patients, the LOD score increased over the first 72 hours.

Effect on life after ICU discharge

Fifty-four (52%) patients were discharged alive from the hospital and followed for a median time of 177 [57-384] days. Among them, 6 (11%) never returned home; 40 (74%) spent more than 50% and 33 (61%) more than 75% of the follow-up time at home; and 15 (28%) were not readmitted during follow-up except for scheduled treatments.

DISCUSSION

Although our patients with nonresectable lung cancer had acceptable rates of ICU and in-hospital survival (69% and 52%, respectively), survival rates were substantially lower after 90 days and 1 year (37% and 12%, respectively). Patients with lung cancer who had a poor ECOG-PS at baseline or who developed multiorgan failure early after ICU admission had significantly higher mortality rates.

Nevertheless, our data suggest that ICU admission may produce meaningful benefits in some patients. Although we did not measure their quality of life, the patients who were discharged alive from the hospital spent most of their time at home. Previous studies of lung cancer patients conducted in recent years (2006-2008) showed ICU mortality rates of 22% to 44%.[11-13] Over the last decade, advances in both oncology and intensive care have improved survival in cancer patients with critical illnesses. Before 2004, ICU mortality rates ranged from 73% to 85%.[14,15] The survival gains are probably ascribable to improvements in the ICU

management of critically ill cancer patients and in the selection of cancer patients for ICU admission.[6,16]

Strengths of our study consist of the relatively large size of the cohort recruited at three centers, exclusion of postoperative patients, and 1-year follow-up data available for nearly all patients. Since lung cancer patients are often considered too sick to benefit from ICU management and are therefore rarely referred for ICU admission (except for immediate post-operative care), 103 patients constitute a good-sized cohort. Other studies have evaluated lung cancer patients admitted to the ICU.[6,12,13,17] but this study is the first to provide data on LOD changes over time. The retrospective design is a weakness. Although the study involved several centers, two of these centers are specialized in treating cancer patients and the third is a university hospital. The management of lung cancer patients in these centers may not accurately reflect usual care. Furthermore, we included only patients who were admitted to the ICU. These patients represent a selected population of patients who are expected to benefit from ICU admission and whose prognosis is therefore better than that in the overall population of patients with nonresectable lung cancer. In addition, the decision to admit patients to the ICU may be subject to the biases of individual physicians. We do not know the extent to which mortality was influenced by the decision to admit patients to the ICU as opposed to the natural history of the disease. A prospective study is needed to evaluate triage policies and prognosis in all lung cancer patients with organ failures.

The challenge, therefore, is to identify those lung cancer patients who are likely to benefit from ICU admission. Performance status and severity of the acute critical illness (SAPS II or LOD score) were the main prognostic factors in our study.[18-20] By multivariate analysis with the LOD score in the model, we found that 90-day mortality was affected by the ECOG-PS, presence of metastatic disease.[11] and LOD score >3 at ICU admission.[11,18] In a retrospective study of cancer patients admitted to the ICU in 2001-2005, the only variable

independently associated with 30-day mortality was an ECOG-PS of 3-4.[21] It is also interesting to note the parallel with the eligibility to chemotherapy when ECOG-PS <3[22,23]. Cancer spread had a smaller impact.[12,24] although the presence of metastatic disease was independently associated with mortality. Interestingly, adequate tumor control as evaluated by the oncologists was not associated with mortality. Tumor-related factors had a considerably smaller impact on the prognosis of critically ill patients with advanced cancer than factors related to the acute disease.[25,26] Severity scores (SAPS II and Acute Physiology And Chronic Health Evaluation [APACHE II]) at ICU admission have been extensively studied and often found to be associated with mortality. Nevertheless, these scores perform poorly for making ICU-admission or other treatment decisions in individual patients.[27] In a prospective study, only 20% of doctors' predictions about the survival of terminally ill patients were accurate; 63% of predictions were overoptimistic and 17% overpessimistic.[28] Interestingly, among mechanically ventilated patients, noninvasive ventilation was associated with a lower mortality rate.[29] A study of 23 cancer patients receiving palliative care and experiencing severe acute respiratory failure showed that noninvasive ventilation was successful in ensuring resolution of the acute episode provided the cause of the respiratory failure was reversible.[30] Survival results from a database study of critically ill cancer patients indicate that the use of mechanical ventilation should generally not be restricted.[31] However, the study population was composed chiefly of surgical patients, and the encouraging results may not apply to other cancer patients.

In cancer patients without factors indicating that ICU management would be futile, a reasonable strategy consists in ICU admission with unrestricted care for a limited period of time, after which the patient's situation is reappraised, if the patient and/or family are willing.[31,32] After 48-72 hours, the treatment strategy should be re-evaluated based on the response to unrestricted management. In our study, an LOD score higher than 6 after 48 hours

was associated with death, except in 3 patients whose organ dysfunctions were stabilized but who still required dialysis on day 3. Thus, an LOD score higher than 6 suggests that life-supporting treatment may not be beneficial. In addition to the absolute LOD score value, the change over time is of interest. A decrease in the LOD score over the first 48 hours was associated with ICU survival in 92% of patients, compared to only 55% of patients whose LOD score increased.

CONCLUSIONS

In a selected population of patients with nonresectable lung cancer, ICU admission was followed by a 52% hospital survival rate. This survival rate is similar to that reported in ICU patients with any type of malignant disease. Factors associated with survival were a good performance status, nonmetastatic disease, and an admission LOD score no higher than 3. ECOG-PS was the main prognostic factor, except when the acute disease was very severe. This study provides the first data on the course of organ dysfunction over the first 3 ICU days in patients with nonresectable lung cancer. Further LOD deterioration over the first 3 days suggests a need for considering treatment-limitation decisions.

REFERENCES

1 Jemal A, Siegel R, Ward E, et al. Cancer statistics, 2009. CA Cancer J Clin 2009; 59:225-249

2 Reck M, von Pawel J, Zatloukal P, et al. Phase III trial of cisplatin plus gemcitabine with either placebo or bevacizumab as first-line therapy for nonsquamous non-small-cell lung cancer: AVAil. J Clin Oncol 2009; 27:1227-1234

3 Shepherd FA, Rodrigues Pereira J, Ciuleanu T, et al. Erlotinib in previously treated non-small-cell lung cancer. N Engl J Med 2005; 353:123-132

4 Garrouste-Orgeas M, Montuclard L, Timsit JF, et al. Predictors of intensive care unit refusal in French intensive care units: a multiple-center study. Crit Care Med 2005; 33:750-755

5 Schapira DV, Studnicki J, Bradham DD, et al. Intensive care, survival, and expense of treating critically ill cancer patients. Jama 1993; 269:783-786

6 Soubani AO, Adam AK. Medical intensive care for lung cancer patients: better than we thought? Future Oncol 2008; 4:141-144

7 Nelson JE, Meier DE, Oei EJ, et al. Self-reported symptom experience of critically ill cancer patients receiving intensive care. Crit Care Med 2001; 29:277-282

8 Naruke T, Tsuchiya R, Kondo H, et al. Implications of staging in lung cancer. Chest 1997; 112:242S-248S

9 Oken MM, Creech RH, Tormey DC, et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. Am J Clin Oncol 1982; 5:649-655

10 Akaike H. A new look at the statistical model identification. IEEE Trans. Automat. Control AC 1974; 19:716-723

11 Adam AK, Soubani AO. Outcome and prognostic factors of lung cancer patients admitted to the medical intensive care unit. Eur Respir J 2008; 31:47-53

12 Soares M, Darmon M, Salluh JI, et al. Prognosis of lung cancer patients with life-threatening complications. Chest 2007; 131:840-846

13 Reichner CA, Thompson JA, O'Brien S, et al. Outcome and code status of lung cancer patients admitted to the medical ICU. Chest 2006; 130:719-723

14 Boussat S, El'rini T, Dubiez A, et al. Predictive factors of death in primary lung cancer patients on admission to the intensive care unit. Intensive Care Med 2000; 26:1811-1816

15 Ewer MS, Ali MK, Atta MS, et al. Outcome of lung cancer patients requiring mechanical ventilation for pulmonary failure. Jama 1986; 256:3364-3366

16 Pene F, Percheron S, Lemiale V, et al. Temporal changes in management and outcome of septic shock in patients with malignancies in the intensive care unit. Crit Care Med 2008; 36:690-696

17 Jennens RR, Rosenthal MA, Mitchell P, et al. Outcome of patients admitted to the intensive care unit with newly diagnosed small cell lung cancer. Lung Cancer 2002; 38:291-296

18 Azoulay E, Moreau D, Alberti C, et al. Predictors of short-term mortality in critically ill patients with solid malignancies. Intensive Care Med 2000; 26:1817-1823

19 Thyrault M, Oppon J, Le Bourdiec S, et al. [Resuscitation management of patients with primary bronchopulmonary cancer]. Presse Med 2002; 31:1446-1450

20 Toffart AC, Pluquet E, Timsit JF, et al. [Bronchial carcinoma and intensive care]. Rev Pneumol Clin 2008; 64:250-256

21 Christodoulou C, Rizos M, Galani E, et al. Performance status (PS): a simple predictor of short-term outcome of cancer patients with solid tumors admitted to the intensive care unit (ICU). Anticancer Res 2007; 27:2945-2948

22 Lilenbaum RC, Cashy J, Hensing TA, et al. Prevalence of poor performance status in lung cancer patients: implications for research. J Thorac Oncol 2008; 3:125-129

23 Moro-Sibilot D, Pluquet E, Zalcman G, et al. [What treatment for a patient of PS 2-3 with stage IV non-small cell lung cancer?]. Rev Mal Respir 2007; 24:6S120-124

24 Blot F, Guiguet M, Nitenberg G, et al. Prognostic factors for neutropenic patients in an intensive care unit: respective roles of underlying malignancies and acute organ failures. Eur J Cancer 1997; 33:1031-1037

25 Glare P, Sinclair C, Downing M, et al. Predicting survival in patients with advanced disease. Eur J Cancer 2008; 44:1146-1156

26 Maltoni M, Caraceni A, Brunelli C, et al. Prognostic factors in advanced cancer patients: evidence-based clinical recommendations--a study by the Steering Committee of the European Association for Palliative Care. J Clin Oncol 2005; 23:6240-6248

27 Staudinger T, Stoiser B, Mullner M, et al. Outcome and prognostic factors in critically ill cancer patients admitted to the intensive care unit. Crit Care Med 2000; 28:1322-1328

28 Christakis NA, Lamont EB. Extent and determinants of error in doctors' prognoses in terminally ill patients: prospective cohort study. Bmj 2000; 320:469-472

29 Azoulay E, Alberti C, Bornstain C, et al. Improved survival in cancer patients requiring mechanical ventilatory support: impact of noninvasive mechanical ventilatory support. Crit Care Med 2001; 29:519-525

30 Cuomo A, Delmastro M, Ceriana P, et al. Noninvasive mechanical ventilation as a palliative treatment of acute respiratory failure in patients with end-stage solid cancer. Palliat Med 2004; 18:602-610

31 Kongsgaard UE, Meidell NK. Mechanical ventilation in critically ill cancer patients: outcome and utilisation of resources. Support Care Cancer 1999; 7:95-99

32 Schonfeld N, Timsit JF. Overcoming a stigma: the lung cancer patient in the intensive care unit. Eur Respir J 2008; 31:3-5

Table 1: Main patient characteristics

	All patients (n=103)	Alive at 90 days (n=35)	Died within 90 days (n=61)	Lost to follow-up* (n=7)
Demographic status				
Male gender	79 (77)	29 (37**)	45 (57)	5 (6)
Age, yr	61 (54-68)	60 (52-67)	61 (54-69)	67 (55-72)
Performance status (missing 1)				
0-2	76 (75)	30 (39)	41 (54)	5 (7)
3-4	26 (253)	5(19)	20 (77)	1 (4)
Modified Charlson Co-morbidity Index	1 (0-2)	1 (0-3)	1 (0-2)	2 (1-3)
Cancer history				
Type of cancer				
- squamous-cell carcinoma	33 (32)	11 (33)	18 (55)	4 (12)
- adenocarcinoma	26 (25)	7 (27)	18 (69)	1 (4)
- small-cell lung cancer	21 (20)	9 (43)	11 (52)	1 (5)
- large-cell lung cancer	11 (11)	4 (36)	6 (55)	1 (9)
- other	12 (12)	4 (33)	8 (67)	0 (0)
Extensive disease (missing 1)				
- No (I-IIIa)	26 (25)	11 (42)	13 (50)	2 (8)
- Yes (IIIb-IV)	76 (75)	24 (32)	47 (62)	5 (6)
metastasis at ICU admission	63 (61)	15 (24)	42 (67)	6 (9)
cancer status				
- not yet treated	23 (22)	8 (35)	14 (61)	1 (4)
- first-line treatment ongoing	31 (30)	13 (42)	16 (52)	2 (6)
- controlled	11 (11)	5 (46)	4 (36)	2 (18)
- recurrence/progression	20 (19)	6 (30)	14 (70)	0 (0)
- diagnosed in the ICU	18 (18)	3 (17)	13 (72)	2 (1)
previous anticancer treatments				
- chemotherapy	59 (57)	23 (39)	32 (54)	4 (7)
- radiation therapy	16 (16)	9 (56)	7 (44)	0 (0)
- surgery	17 (1)	8 (47)	7 (41)	2 (12)
- no previous anticancer treatment	41 (49)	11 (27)	27 (66)	3 (7)
time since cancer diagnosis (days)	95 (25-251)	152 (40-276)	86 (24-182)	150 (1-1010)

Data are median (interquartile range) for quantitative data and number (%) for qualitative data.

(*) 7 patients were censored after less than 3 months of follow-up.

(**) % of the overall population for this characteristic

Table 2: Characteristics of the critical illnesses

	All patients (n=103)	Alive at 90 days (n=35)	Died within 90 days (n=61)	Lost to follow-up* (n=7)
Reasons for ICU admission				
Acute respiratory failure	58 (56)	21 (36**)	34 (59)	3 (5)
- infection	18 (31)	3 (17)	14 (78)	1 (5)
- airway obstruction	9 (16)	3 (33)	4 (45)	2 (22)
. obstruction by the tumor	7 (78)	2 (29)	4 (57)	1 (14)
- superior vena cava syndrome	2 (3)	0 (0)	2 (100)	0 (0)
- pneumothorax	7 (12)	5 (71)	2 (29)	0 (0)
- pulmonary embolism	4 (7)	1 (25)	3 (75)	0 (0)
- pleural effusion	4 (7)	1 (25)	3 (75)	0 (0)
- hemoptysis	4 (7)	1 (25)	3 (75)	0 (0)
- acute pulmonary edema	4 (7)	4 (100)	0 (0)	0 (0)
- other	6 (10)	3 (50)	3 (50)	0 (0)
shock	27 (26)	7 (26)	17 (63)	3 (11)
- septic	11 (41)	1 (9)	9 (82)	1 (9)
- cardiogenic	6 (22)	2 (33)	3 (50)	1 (17)
- other	10 (37)	4 (40)	5 (50)	1 (10)
Neurologic complications	7 (7)	3 (43)	3 (43)	1 (14)
Other	11 (11)	4 (36)	7 (64)	0 (0)
LOD score	3 (1-4)	1(0-4)	3 (1-4)	3 (1-5)
number of organ failures	1 (1-2)	1 (0-1)	2 (1-2)	1 (1-3)
SAPS II	33 (25-46)	26 (22-35)	36 (30-52)	33 (26-46)
Treatments during the first 48 hours				
- noninvasive ventilation	20 (19)	8 (40)	11 (55)	1 (5)
- invasive ventilation	41 (40)	9 (22)	30 (73)	2 (5)
- vasoactive drugs	33 (32)	7 (21)	25 (76)	1 (3)
- renal replacement therapy	5 (5)	2 (40)	3 (60)	0 (0)
LOD score on day 3	2 (0-5)	1 (0-4)	3 (1-10)	2 (1-5)
number of organ failures on day 3	1 (0-3)	1 (0-1)	2 (1-2)	1 (1-2)
length of ICU stay (days)	3 (2-7)	4 (2-7)	3 (1-7)	3 (2-6)
length of hospital stay (days)	9 (2-20)	12 (6-22)	6 (2-19)	9 (15-23)

Data are median (interquartile range) for quantitative data and number (%) for qualitative data.

(*) 7 patients were censored after less than 3 months of follow-up.

(**) % of the overall population for this characteristic

Table 3: Univariate and multivariate analysis of factors associated with 90-day mortality

	Univariate* analysis HR [95% CI], *P* value	**Multivariate* analysis (model with SAPS II) HR [95% CI], *P* value**	**Multivariate analysis (model with LOD) HR [95% CI], *P* value**
Demographic features			
Age >61 years	1.00 [0.60-1.67], 0.98		
Male	0.74 [0.41-1.32], 0.31		
Performance status >2	1.91 [1.10-3.33], 0.02	1.96 [1.11-3.46], 0.02	2.65 [1.43-4.88], $<10^{-2}$
CCI, modified	0.61 [0.31-1.16], 0.14		
Cancer history			
Cancer status			
- not yet treated	1.15 [0.63-2.13], 0.64		
- first-line treatment ongoing	0.87 [0.48-1.56], 0.64		
- controlled	1.01 [0.61-1.67], 0.98		
- recurrence/progression	1.17 [0.62-2.22], 0.63		
- diagnosed in the ICU	1.09 [0.58-2.03], 0.79		
Metastasis at ICU admission	2.00 [1.14-3.49], 0.01		1.90 [1.08-3.33], $<10^{-2}$
Cancer diagnosis for >90 days	0.94 [0.56-1.59], 0.82		
Cancer excision surgery	0.68 [0.32-1.45], 0.32		
Reasons for ICU admission			
- acute respiratory failure**	0.90 [0.55-1.5], 0.70		
- shock	1.40 [0.79-2.50], 0.25		
Treatments in the 1st 72 hours			
- invasive ventilation	1.90 [1.13-3.19], 0.02		
- noninvasive ventilation	0.83 [0.45-1.53], 0.54		
- vasoactive drugs	2.27 [1.33-3.87], $<10^{-2}$		
Scores at ICU admission			
LOD, per point	1.17 [1.05-1.29], $<10^{-2}$		1.19 [1.08-1.32], $<10^{-3}$
LOD >3	1.99 [1.18-3.38], 0.01		
SAPS II, per point	1.03 [1.02-1.05], $<10^{-4}$	1.03 [1.02-1.05], 10^{-4}	

The Akaike information criterion of the model was 376.1 with SAPS II and 366.9 with the LOD score in the model.

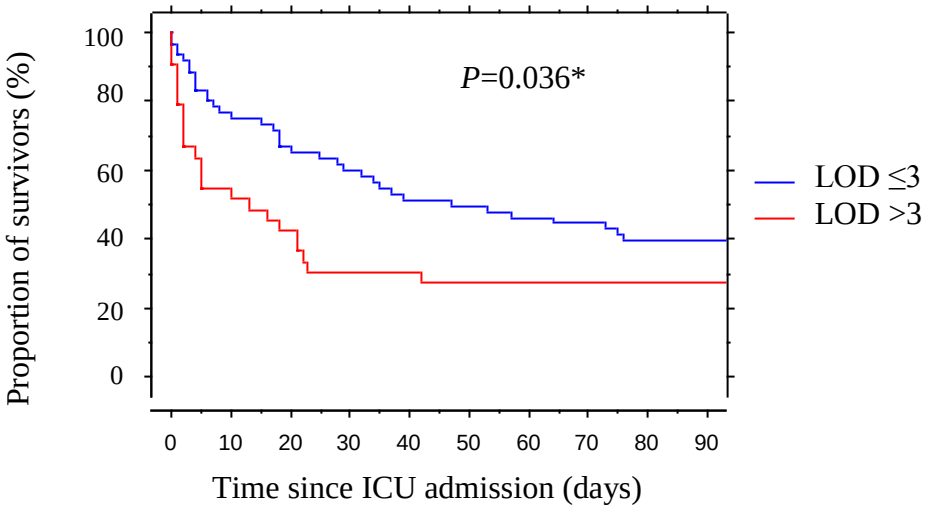
(*) Analysis stratified by center

(**) refers to the category in Table 2

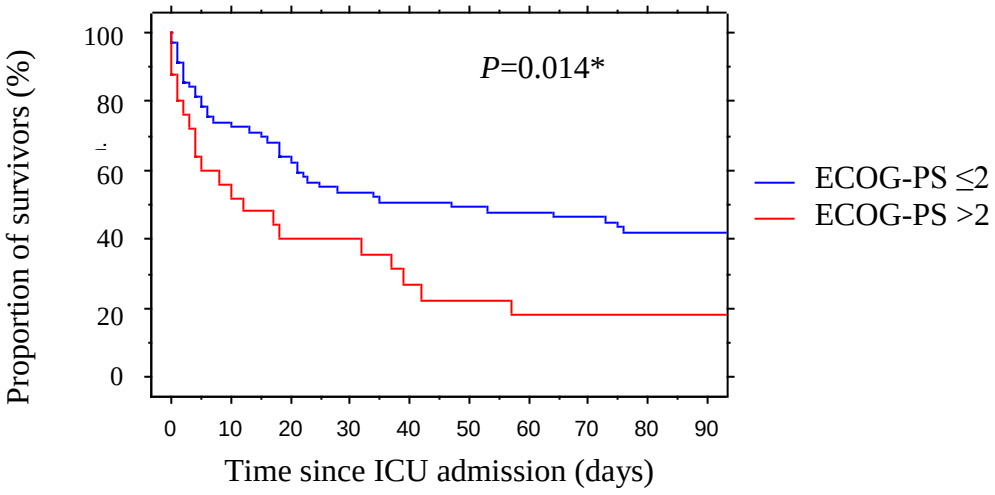
Figure 1: Probability of survival at 90 days according to LOD (A) or ECOG-PS (B)

Kaplan-Meier curve of survival in patients with nonresectable lung cancer admitted to the ICU, according to acute-illness severity at ICU admission (Logistic Organ Dysfunction score) and ECOG-PS

A



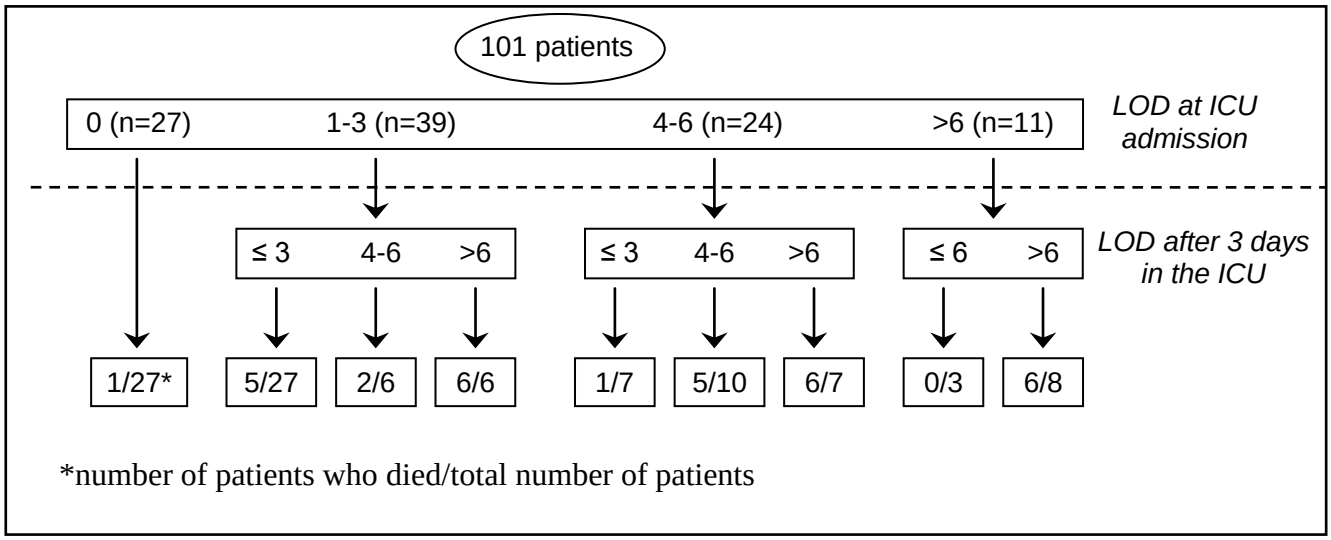
B



*log-rank test

Figure 2: ICU mortality according to LOD score evolution (2 missing data)

Description of the characteristics of the LOD scores at ICU admission and after 3 days in the ICU.



*number of patients who died/total number of patients

Conclusion

THESE SOUTENUE PAR : Anne-Claire TOFFART

TITRE : Prise en charge en réanimation de patients porteurs d'un cancer bronchique non résécable

CONCLUSION

Dans une population sélectionnée de patients porteurs d'un cancer bronchique non résécable, l'admission en réanimation a été suivie d'un taux de survie hospitalière de 52%. Ce taux de survie était similaire à ceux rapportés quelque soit le type de tumeur maligne. Les facteurs associés à la survie étaient un bon performance status, une maladie non métastatique et un LOD score à l'admission inférieur ou égal à 3. L'ECOG-PS était le principal facteur pronostique, si l'on exclut une maladie aiguë très sévère. Cette étude est la 1ère à apporter des informations concernant l'évolution des défaillances d'organe après 3 jours de prise en charge en réanimation des patients porteurs d'un cancer bronchique non résécable. Une aggravation du LOD score sur les trois 1ers jours suggère la nécessité de reconsidérer une éventuelle limitation thérapeutique.

VU ET PERMIS D'IMPRIMER
Grenoble, le 29/04/2010

LE DOYEN

B.SELE

FACULTE DE MEDECINE - UNIVERSITE JOSEPH FOURIER GRENOBLE 1 - FACULTÉ DE MÉDECINE SCOLARITÉ

LE PRESIDENT DU JURY

D. MORO-SIBILOT

SERMENT D'HIPPOCRATE

En présence des Maîtres de cette Faculté, de mes chers condisciples et devant l'effigie d'HIPPOCRATE,

je promets et je jure d'être fidèle aux lois de l'honneur et de la probité dans l'exercice de la Médecine.

Je donnerai mes soins gratuitement à l'indigent et n'exigerai jamais un salaire au dessus de mon travail. Je ne participerai à aucun partage clandestin d'honoraires.

Admis dans l'intimité des maisons, mes yeux n'y verront pas ce qui s'y passe ; ma langue taira les secrets qui me seront confiés et mon état ne servira pas à corrompre les mœurs, ni à favoriser le crime.

Je ne permettrai pas que des considérations de religion, de nation, de race, de parti ou de classe sociale viennent s'interposer entre mon devoir et mon pâtient.

Je garderai le respect absolu de la vie humaine.

Même sous la menace, je n'admettrai pas de faire usage de mes connaissances médicales contre les lois de l'humanité.

Respectueux et reconnaissant envers mes Maîtres, je rendrai à leurs enfants l'instruction que j'ai reçue de leurs pères.

Que les hommes m'accordent leur estime si je suis fidèle à mes promesses.

Que je sois couvert d'opprobre et méprisé de mes confrères si j'y manque.