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Factors affecting survival after palliative radiotherapy in patients with lung cancer

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ABSTRACT

Background: Lung cancer is the most common cancer worldwide. It is estimated that 60% of patients with NSCLC at time of diagnosis have advanced disease. The aim of this study was to identify factors that play a major role in the survival of lung cancer patients treated with palliative radiotherapy.

Materials and methods: We retrospectively reviewed data of 280 lung cancer patients treated with palliative radiotherapy from January 2013 to December 2017. A multivariate analysis using the proportional hazards model of Cox was conducted. Also, Kaplan Meier curves were used to describe the distribution of survival times of the patients. The level of significance was set at 0.05.

Results: The mean age at diagnosis was 65.6 years. About 77.5% of patients were male and 22.5% were female. In our cohort > 95% had stage 4 lung cancer. Most cases were adenocarcinomas (72.5%) and ECOG-PS 0–1 (80.4%). Different sites were submitted to palliative treatment: 120 brain metastases, 96 bone metastases, 53 lung tumour, 8 lymph nodes and 3 lung metastases. Brain as first site of palliative radiotherapy (HR: 1.553, 95% CI: 1.167–2.067, $p = 0.003$) and ECOG-PS 2–3 compared with ECOG-PS 0–1 (HR: 2.253, 95% CI: 1.546–3.283, $p \leq 0.001$) were associated with increased likelihood of lung cancer death. Patients who received biological therapy had 70.7% ($p \leq 0.001$) reduction in lung cancer death risk.

Conclusion: Brain as the first metastatic site treated with radiotherapy and ECOG-PS 2–3 are associated with increased lung cancer death. Biological therapy was associated with decreased death risk.

Key words: lung neoplasms; radiotherapy; palliative therapy

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Introduction

Lung cancer accounts for 12% of all cancers and has the highest annual rate of mortality in men and women [1]. Almost 60% of patients at the moment of diagnosis are not eligible for radical treatment [2–5].

Standard treatment options may include palliative external beam radiation therapy, in combination with chemotherapy or with chemotherapy and biological therapy, and any laser therapy or brachytherapy if needed [2, 5, 6].

Palliative radiotherapy may be used in different metastatic sites, osseous, cerebral, subcutaneous, nodal, or pulmonary to improve the quality of life and minimize symptoms [4]. Thoracic radiotherapy is a cornerstone in management of advanced stage III and IV lung cancer patients [7, 8] and bone radiotherapy is a successful method to palliate pain and/or prevent morbidity [9, 10].

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The purpose of this study was to identify factors that play a major role in the survival of lung cancer patients treated with palliative radiotherapy for the first time in our department.

Materials and methods

This study is a retrospective analysis of patients from a single academic hospital (Centro Hospitalar Universitário de São João in Porto, Portugal). This study was approved by the institutional ethical review board (reference number: 204/19). All lung cancer patients treated with first course of palliative radiotherapy between January 2013 and December 2017 were included (n = 280). Electronic health records were collected in February 2019. Follow-up time was defined as the time between date of radiotherapy and date of death or last clinical visit. Lung cancer specific survival was defined as the time from the date of first radiotherapy course to the date of death from lung cancer.

The Chi-square (χ^2) test was used to compare the clinicopathological features among different sites of metastases. The distribution of the lung cancer specific survival was estimated by the Kaplan-Meier method. We performed the log-rank test to analyse variables for lung cancer specific survival, considering the following variables of interest: age (< 70 years old *vs.* ≥ 70), ECOG-PS (0–1 *vs.* 2–3), smoking, alcohol, gastro-intestinal disease, lung disease, cardiac disease, hypertension, diabetes mellitus, stage, pathology, palliative RT localization (brain vs other), surgery, chemotherapy, biological therapy and further course of radiotherapy. RT characteristics including dose per fraction and number of fractions were used to quantify equivalent dose in 2Gy per fraction (EQD_2, alpha/beta = 10).

We evaluated acute toxicity by Toxicity criteria of the Radiation Therapy Oncology Group (RTOG) [11].

Cox proportional hazards regression modelling was used to assess the outcome of death caused by lung cancer, adjusted for significant clinical covariates. The covariates were the following: age (< 70 years old *vs.* ≥ 70), ECOG-PS (0–1 *vs.* 2–3), biological therapy, chemotherapy, palliative RT localization (brain vs other), gastro-intestinal disease, lung disease, cardiac disease, hypertension, diabetes mellitus, smoker, alcohol and further course of radiotherapy. We presented graphically the curves of lung cancer specific survival. All analyses were performed using an IBM® SPSS® Statistics V25 and, for all, a level of significance $\alpha = 0.05$ was noted.

Results

In our department, between January 2013 and December 2017, we treated 280 lung cancer patients with the first course of palliative radiotherapy without previous irradiation.

The most common irradiated metastatic sites were the brain (43%) and bone metastases (34%).

Most patients were diagnosed at the stage IVA ($p < 0.001$) and predominant histology was adenocarcinoma ($p = 0.003$) among different sites of metastases.

Patients with lung tumour were more likely to receive pathological confirmation ($p < 0.001$), unlike brain and bone metastases. Further course of radiotherapy was more frequent for bone metastases than other metastasis sites ($p < 0.001$).

The clinical characteristics were summarized in Table 1.

During the course of the disease, patients were submitted to other treatments, such as surgery, chemotherapy, biological therapy (immune checkpoint inhibitors or tyrosine kinase inhibitors), illustrated in Table 1.

We irradiated different sites of bone metastases, as illustrated in Table 2. Most of them were vertebral metastases (n = 48, 50%) followed by pelvic metastases (n = 15, 15.6%). The radiotherapy goal was to control the pain (n = 93, 96.9%) and we irradiated 3 spinal cord compressions.

On palliative irradiation of the lung tumour, the main goal was to control pain (n = 30, 56.6%) followed by growth control (n = 13, 24.5%). On irradiation of the lymph nodes, most of them were on the mediastinum (n = 4) followed by the axilla (n = 3) and the main goal was growth control (n = 4, 50%).

Total radiotherapy doses varied between 8 and 45 Gy and all patients were treated with 3D conformal radiation therapy. Different radiotherapy schemes were performed according with symptomatology and localization. The most common dose fractionation for brain and bone metastases was 30 Gy in 10 fractions and 40 Gy in 16 fractions on lymph nodes. Most of lung tumour and lung metastases were submitted to 45 Gy in 18 fractions and 40 Gy in 16

Table 1. Patient, tumour and treatment characteristics (n = 280)

Variable	Brain (n = 120)	Bone (n = 96)	Lung tumour (n = 53)	Lymph node metastases (n = 8)	Lung metastases (n = 3)	p-value
Gender						
Male	87 (72.5)	77 (80.2)	43 (81.1)	7 (87.5)	3 (100)	0.426
Female	33 (27.5)	19 (19.8)	10 (18.9)	1 (12.5)	0 (0.0)	
Age (years old)						
< 70	85 (70.8)	39 (40.6)	27 (66.7)	5 (62.5)	2 (66.7)	0.135
≥ 70	35 (29.2)	57 (59.4)	26 (49.1)	3 (37.5)	1 (33.3)	
ECOG-PS						
0–1	97 (80.8)	78 (81.3)	42 (79.2)	6 (75.0)	2 (75.0)	0.962
2–3	23 (19.2)	18 (18.8)	11 (20.8)	2 (25.0)	1 (33.3)	
Habits						
Alcohol	42 (35.0)	21 (21.9)	16 (30.2)	4 (50.0)	2 (66.7)	0.981
Smoker/ex-smoker	94 (78.3)	73 (76.0)	43 (81.1)	6 (75.0)	3 (100)	0.841
Comorbidities						
Gastrointestinal	17 (14.2)	13 (13.5)	2 (3.8)	2 (25.0)	0 (0.0)	0.217
Lung disease	22 (18.3)	14 (14.6)	13 (24.5)	1 (12.5)	1 (33.3)	0.574
Heart disease	21 (17.5)	15 (15.6)	10 (18.9)	1 (12.5)	0 (0.0)	0.908
Hypertension	49 (40.8)	38 (39.6)	26 (49.1)	3 (37.5)	1 (33.3)	0.820
Diabetes mellitus	17 (14.2)	12 (12.5)	12 (22.6)	1 (12.5)	1 (33.3)	0.449
Stage (AJCC 8th)						
IIIA	0 (0.0)	0 (0.0)	2 (3.8)	0 (0.0)	0 (0.0)	
IIIB	0 (0.0)	0 (0.0)	4 (7.5)	0 (0.0)	0 (0.0)	< 0.001
IVA	107 (89.2)	62 (64.6)	46 (86.8)	6 (75.0)	3 (100)	
IVB	13 (10.8)	34 (35.4)	1 (1.9)	2 (25.0)	0 (0.0)	
Pathology						
Adenocarcinoma	93 (77.5)	76 (79.2)	25 (47.2)	6 (75.0)	3 (100)	
Neuroendocrine	16 (13.3)	9 (9.4)	15 (28.3)	1 (12.5)	0 (0.0)	0.003
Epidermoid	8 (6.7)	11 (11.5)	13 (24.5)	1 (12.5)	0 (0.0)	
Other	3 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
Biopsy						
Yes	4 (3.3)	0 (0.0)	50 (94.3)	4 (50.0)	3 (100)	< 0.001
No	116 (96.7)	96 (100)	3 (5.7)	4 (50.0)	0 (0.0)	
Further course of radiotherapy						**0.002**
Yes	12 (10.0)	27 (28.1)	3 (5.7)	1 (12.5)	0 (0.0)	
No	108 (90.0)	69 (71.9)	50 (94.3)	7 (87.5)	3 (100)	
Surgery						
Yes	7 (5.8)	9 (9.4)	2 (3.8)	0 (0.0)	0 (0.0)	0.586
No	113 (94.2)	87 (90.6)	51 (96.2)	8 (100)	3 (100)	
Chemotherapy						
Yes	116 (96.7)	94 (97.9)	50 (94.3)	8 (100)	3 (100)	0.775
No	4 (3.3)	2 82.1)	3 (5.7)	0 (0.0)	0 (0.0)	
Biological therapy						
Yes	28 (23.3)	24 (25.0)	10 (18.9)	2 (25.0)	0 (0.0)	0.799
No	92 (76.7)	72 (75.0)	43 (81.1)	6 (75.0)	3 (100)	
Current state						
Alive	11 (9.2)	11 (11.5)	5 (9.4)	0 (0.0)	0 (0.0)	0.973
Dead	108 (90.0)	84 (87.5)	48 (90.6)	8 (100)	3 (100)	
Unknown	1 (0.8)	1 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)	

ECOG-PS — Eastern Cooperative Oncology Group Performance Status; AJCC — American Joint Committee on Cancer; *Table XX illustrated type of bone

Table 2. Bone and lymph metastases and lung tumour characteristics treated with palliative radiotherapy

Metastases	n (%)	Radiotherapy intention, n(%)
Bone Metastases	96 (100)	
Vertebral	48 (50.0)	Spinal cord descompression, 3 (3.1)
Pelvis	15 (15.6)	
Rib	13 (13.5)	
Long bone	12 (12.5)	Pain control, 93 (96.9)
Shoulder girdle	5 (5.2)	
Sternum	2 (2.1)	
Shaw	1 (1.0)	
Lung tumour	53 (100)	
Superior lobe	19 (35.8)	Pain control, 30 (56.6)
Inferior lobe	10 (18.9)	Growth control,13 (24.5)
Medium lobe	1 (1.9)	SCVS, 5 (9.4)
Hilo/mediastinum	23 (43.4)	Hemorrhagic control, 4 (7.5)
Lymph node metastases	8 (100)	
Mediastinum	4 (50.0)	Growth control, 4 (50.0)
Axilla	3 (37.5)	Pain control, 2 (25.0)
Cervical	1 (12.5)	SCVS, 2 (25.0)

Chem — chemotherapy; Immu — immunotherapy; TKIs — tyrosine kinase inhibitors; SCVS — superior vena cava syndrome

fractions. Treatment characteristics are detailed in Table 3.

In terms of EQD2 (α/β = 10), we presented the value in accordance with metastases localization. For lung tumour and lung metastases doses varied between 31.25 to 46.88 Gy and 41.67 Gy, respectively. Dose to brain metastases varied between 12.0 and 32.5 Gy and most of patients received 30 Gy in 10 fractions (74.2%). The scheme most applied to bone metastases was 30 Gy in 10 fractions (37.5%), dose range of 12.0 to 41.67 Gy. We treated 8 lymph nodes metastases with a dose range of 23.3 to 46.88 Gy.

Table 4 illustrates radiotherapy acute toxicity according to the site of metastasis. With lung radiotherapy the most common toxicities were grade 1 RTOG.

Brain radiotherapy revealed grade 1 RTOG in the skin (n = 10, 8.3%). In patients undergoing bone radiotherapy, revealed grade 1 RTOG in the skin (n = 4, 4.2%) and in patients whose radiotherapy field included the lung, grade 1 RTOG in the lung was documented in 7 patients (1.3%).

The median follow-up time was 5 months (IQR = 11). The univariate analysis indicated that ECOG 0–1 *vs.* ECOG 2–3 (median 16.8 months (95% CI: 13.5–20.0) *vs.* 5.3 months (95% CI: 3.5–37.2), p < 0.001), chemotherapy (median 15.3 months (95% CI: 12.4–18.2) *vs.* 3.7 months (95% CI:

Table 3. Radiotherapy dose treatment characteristics

Localization	Total dose/ /fraction nº	n (%)
Lung tumour	30/10	11 (20.8)
	30/12	2 (3.8)
	40/15	1 (1.9)
	40/16	8 (15.1)
	45/18	31 (58.5)
EQD_2 (alpha/beta = 10)	Median (range)	46.88 (31.25–46.88)
Lung metastases	40/16	3 (100)
EQD_2 (alpha/beta = 10)	Median (range)	41.67 (41.67–41.67)
Brain	18/10	1 (0.8)
	20/5	29 (24.2)
	30/10	89 (74.2)
EQD_2 (alpha/beta = 10)	Median (range)	32.50 (12.00–32.50)
Bone	8/1	9 (9.4)
	20/5	27 (28.1)
	30/10	36 (37.5)
	30/12	13 (13.5)
	30/9	8 (8.3)
	40/16	3 (3.1)
EQD_2 (alpha/beta = 10)	Median (range)	31.25 (12.00–41.67)
Lymph node	20/5	1 (12.5)
	30/10	1 (12.5)
	40/16	3 (37.5)
	45/18	3 (37.5)
EQD_2 (alpha/beta = 10)	Median (range)	41.67 (23.30–46.88)

EQD_2 — equivalent dose in 2 Gy per fraction

Table 4. Radiotherapy toxicity according to site of radiotherapy localization

RTOG grade	Lung n (%)	Brain n (%)	Bone n (%)
RTOG skin			
0	38 (67.9)	109 (90.8)	92 (95.8)
1	17 (30.4)	10 (8.3)	4 (4.2)
2	1 (1.8)	1 (0.8)	–
RTOG Lung			
0	42 (75.0)		89 (92.7)
1	13 (23.2)	NA	7 (1.3)
2	1 (1.8)		–
RTOG gastrointestinal			
0	45 (80.4)		
1	6 (10.7)	NA	NA
2	5 (8.9)		

RTOG — Radiation Therapy Oncology Group; NA — not applicable

0.7–6.7), p = 0.008) and biological therapy (median 32.1 months (95% CI: 24.5–39.7) *vs.* 9.4 months (95% CI: 7.4–11.4), p < 0.001) were correlated with lung cancer specific survival. Patients treated with palliative brain radiotherapy revealed significantly lower lung cancer specific survival when compared to other sites (median 12.9 months (95% CI: 8.9–16.9) *vs.* 15.7 months (95% CI: 12.2–19.2), p = 0.031), illustrated in Table 5 and Figure 1.

Multivariate analysis revealed that brain as the first site of metastasis, ECOG 2–3 and biological therapy were independent prognostic factors for metastatic lung cancer survival.

Patients treated with brain radiotherapy were associated with worst lung cancer specific survival (HR: 1.553, 95% CI: 1.167–2.067, p = 0.003), similar to ECOG 2–3 (HR: 2.253, 95% CI: 1.546–3.283, p < 0.001), whereas patients who had undergone biological therapy presented better lung cancer specific survival, 70.7% (HR: 0.293, 95% CI: 0.197–0.436, p < 0.001) reduction in lung cancer death, as illustrated in Table 6 and Figure 1.

Discussion

The present study explored the characteristics and outcomes of metastatic lung cancer patients undergoing first course of palliative radiotherapy, without previous irradiation.

The median survival rate reported, 5 months, resembles a large clinical trial [2, 3].

We treated 280 patients with palliative radiotherapy and the brain was the most prevalent localization (n = 120) followed by the bone (n = 96). Metastatic sites patterns are globally in accordance with those stated in other studies. Previous studies have shown that the most common metastatic sites in lung cancer are the brain, bone, respiratory system, liver, and adrenal glands [12, 13]. Riihimaki et al (2014) studied 17.431 lung cancer patients diagnosed between 2002 and 2010 and revealed population-based data on metastatic sites. Bone (39%) and respiratory system (22%) metastases were prevalent in adenocarcinoma, which is in accordance with the pathology distribution in our study, where adenocarcinoma was the most prevalent. For small cell cancer they found higher prevalence of nervous system (47%) and liver (35%) metastases [12]. Another study showed a total of 54,687 patients with metastatic lung cancer between 2010 and 2014. The most prevalent were multiple organ metastases (37.2%) followed by bone metastases (20%), lung metastases (17.2%), brain metastases (15.2%) and liver metastases (10.4%) [14].

We applied different doses, in accordance with patient characteristics, treatment localization and department experience. Janssen et al. [15] reported in a retrospective analysis of 125 patients that increasing equivalent dose in 2 Gy fractions (EQD2) led to significantly better survival outcomes. EQD2 of 31–40, 41–46 and 47–52 Gy led to 6-month overall survival of 30, 38 and 57%, respectively, and 1-year overall survival of 11, 26 and 36%, respectively. On multivariable analysis, EQD2 was significant. The doses of radiotherapy described by

Table 5. Results of univariate analysis for lung cancer specific survival

	Lung cancer survival rate at 1 year (%), (months)	Median survival (months)	95% CI	p-value
Age (years old)				
< 70	30.3	14.6	11.3–17.9	0.998
≥ 70	32.2	14.6	9.9–19.2	
ECOG–PS				
0–1	34.5	16.8	13.5–20.0	**< 0.001**
2–3	15.5	5.3	3.5–7.2	
Habits				
Alcohol	29.9	12.8	9.2–16.5	0.904
Smoker	29.1	13.2	10.5–15.9	0.264
Comorbidities				
Gastrointestinal	25.4	12.4	5.6–19.2	0.487
Lung disease	24.8	14.2	8.0–20.3	0.698
Heart disease	27.9	15.3	7.6–22.9	0.950
Hypertension	29.9	11.0	8.3–13.7	0.322
Diabetes mellitus	29.6	16.6	8.0–25.1	0.871
Stage				
IIIA	0.0	12.0	10.0–13.9	
IIIB	0.0	5.3	1.8–8.7	0.698
IVA	29.8	15.1	11.8–18.3	
IVB	38.2	13.8	8.7–18.8	
Pathology				
Adenocarcinoma	33.7	15.9	12.4–19.3	
Neuroendocrine	23.4	11.1	7.3–14.9	0.354
Epidermoid	26.1	11.4	5.8–17.1	
Other	0.0	3.3	0.0–4.0	
Palliative RT localization				
Brain	26.5	12.9	8.9–16.9	**0.031**
Other	34.7	15.7	12.2–19.2	
Surgery				
Yes	50.2	21.7	9.8–33.7	0.141
No	29.1	14.3	11.4–17.1	
Chemotherapy				
Yes	31.9	15.3	12.4–18.2	**0.008**
No	0	3.7	0.7–6.7	
Biological therapy				
Yes	60.0	32.1	24.5–39.7	< 0.001
No	22.1	9.4	7.4–11.4	
Another course of radiotherapy				
Yes	48.3	15.9	20.9–13.0	0.166
No	27.1	14.9	11.7–18.2	

ECOG-PS — Eastern Cooperative Oncology Group – Performance Status; EQD2 — equivalent dose in 2 Gy per fraction; CI — confidence interval

Janseen et al. were higher compared with those used in our study. In addition, Frank et al. [16] investigated 159 patients with NSCLC and compared 30 Gy/10 fractions, 25 Gy/five fractions, 15 Gy/three fractions and 10 Gy/one fraction, finding no statistically significant correlation between overall survival and radiotherapy regimes. It is difficult to directly compare this study with others finding a positive correlation between increased fractionation and overall survival, as the fractionation schemes utilized in each study are variable with a large range in EQD2.

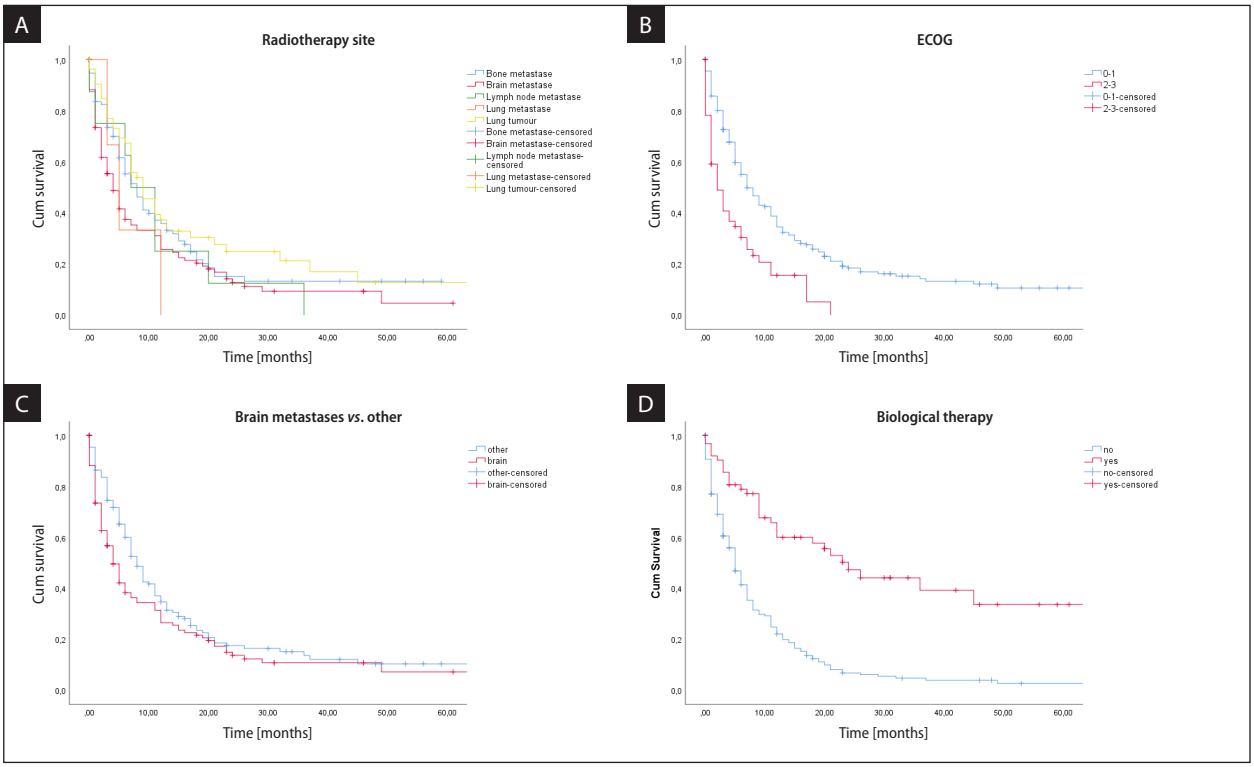

Figure 1. Lung cancer specific survival curves in patients treated with palliative radiotherapy between 2013 and 2017 according to radiotherapy site (**A**), ECOG-PS (**B**), palliative brain radiotherapy vs. other (**C**) and biological therapy (**D**)

Table 6. Results of multivariate analysis for lung cancer specific survival. Multivariate analysis was performed that included clinically important variables and variables with statistical p < 0.05 by the univariate analysis

	p	HR	95% CI for HR	
			Lower	Upper
Age ≥ 70 y/o (ref: < 70 y/o)	0.995	0.999	0.733	1.362
ECOG-PS 2-3 (ref: ECOG-PS 0-1)	< 0.001	2.253	1.546	3.283
Biological therapy (ref: no)	< 0.001	0.293	0.197	0.436
Chemotherapy (ref: no)	0.235	0.630	0.294	1.349
Brain metastases (ref: others)	0.003	1.553	1.167	2.067
Gastrointestinal disease (ref: no)	0.691	1.092	0.707	1.687
Lung disease (ref: no)	0.387	0.850	0.588	1.228
Cardiac disease (ref: no)	0.620	0.905	0.612	1.340
Hypertension (ref: no)	0.389	1.140	0.847	1.534
DM (ref: no)	0.960	0.990	0.662	1.480
Smoker (ref: no)	0.830	1.039	0.732	1.476
Alcohol (ref: no)	0.608	0.922	0.677	1.256
Another course of radiotherapy (ref: no)	0.062	0.693	0.472	1.018

HR — hazard ratio; CI — confidence interval; DM — diabetes mellitus; ECOG-PS — Eastern Cooperative Oncology Group — Performance Status

An optimal radiotherapy regimen palliates symptom with minimal toxicity. In general, the published data regarding toxicity, reveals that treatment was well tolerated [16–18].

In multivariate analysis (Tab. 6), this study revealed that statistically significant factors with survival impact were ECOG 2–3 (p < 0.001), biological therapy (p < 0.001), and brain as first sites of me-

tastases (p = 0.003). Specifically, the risk of lung cancer death with brain metastases was 1.6 times greater than other sites and ECOG 2–3 patients had a risk of lung cancer death 2.3 times greater than ECOG 0–1. The finding that the performance status is significantly correlated with survival is in concordance with other studies [19, 20]. Li et al. (2019), performed a multivariate analysis that included gender, age at diagnosis, race, histology, tumour grade, tumour stage, surgery of metastases, using chemotherapy and radiotherapy and metastases site. All of those were independent prognostic factors for cancer specific survival. They used brain metastases as the reference and patients with isolated bone metastases had similar cancer-specific-survival. In this study, lung metastases represented better cause-specific survival. On the other hand, liver and multisite metastases were associated with worse cause-specific-survival [12, 14].

Riihimaki et al (2014) showed in their publications a five-month median survival after diagnosis for liver and bone metastases as the worst prognosis [12]. The differences of our results may be explained by a lower number of patients.

Most patients in our cohort received other treatments, such as chemotherapy or biological therapy. In our analysis, those treatments were associated with a decrease in lung cancer death risk on univariate analysis. Multivariate analysis revealed greater lung cancer specific survival in patients who had undergone biological therapy. Our study did not take into account the gene expression or checkpoint inhibitors expression; however, the new target therapies and immunotherapy are changing the course of this disease, especially for patients having tumour presenting some gene mutation drivers, like EGFR (21, 22), ALK translocation [23, 24] and ROS arrangement [25, 26] or programmed death ligand 1 (PD-L1) expression [27, 28].

We should acknowledge that there are limitations in our study. It is a retrospective study with heterogeneous metastatic disease patients and there was a lack of details about chemotherapy, biological therapy and gene expression which may cause bias.

Conclusion

In patients with distant metastases treated with palliative radiotherapy at our institution, those with brain metastases have the worse lung cancer specific survival as compared to other metastatic sites. Biological therapy was associated with decreased death risk and better survival.

Conflict of interest

None declared.

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References

1. Carioli G, Bertuccio P, Boffetta P, et al. European cancer mortality predictions for the year 2020 with a focus on prostate cancer. Ann Oncol. 2020; 31(5): 650–658, doi: 10.1016/j.annonc.2020.02.009, indexed in Pubmed: 32321669.
2. Gadgeel S, Rodríguez-Abreu D, Speranza G, et al. Updated Analysis From KEYNOTE-189: Pembrolizumab or Placebo Plus Pemetrexed and Platinum for Previously Untreated Metastatic Nonsquamous Non-Small-Cell Lung Cancer. J Clin Oncol. 2020; 38(14): 1505–1517, doi: 10.1200/JCO.19.03136, indexed in Pubmed: 32150489.
3. Gandhi L, Rodríguez-Abreu D, Gadgeel S, et al. KEYNOTE-189 Investigators. Pembrolizumab plus Chemotherapy in Metastatic Non-Small-Cell Lung Cancer. N Engl J Med. 2018; 378(22): 2078–2092, doi: 10.1056/NEJMoa1801005, indexed in Pubmed: 29658856.
4. Nowicki A, Farbicka P, Krajnik M, et al. Palliative care in patients with lung cancer. Contemp Oncol (Pozn). 2013; 17(3): 238–245, doi: 10.5114/wo.2013.35033, indexed in Pubmed: 24596508.
5. Moumtzi D, Lampaki S, Zarogoulidis P, et al. Prognostic factors for long term survival in patients with advanced non-small cell lung cancer. Ann Transl Med. 2016; 4(9): 161, doi: 10.21037/atm.2016.05.13, indexed in Pubmed: 27275474.
6. Lemjabbar-Alaoui H, Hassan OUi, Yang YW, et al. Lung cancer: Biology and treatment options. Biochim Biophys Acta. 2015; 1856(2): 189–210, doi: 10.1016/j.bbcan.2015.08.002, indexed in Pubmed: 26297204.
7. Jumeau R, Vilotte F, Durham AD, et al. Current landscape of palliative radiotherapy for non-small-cell lung cancer. Transl Lung Cancer Res. 2019; 8(Suppl 2): S192–S201, doi: 10.21037/tlcr.2019.08.10, indexed in Pubmed: 31673524.
8. Shamp S, Patel RB, Biswas T. Palliative Radiation Therapy in Extensive Stage Small Cell Lung Cancer (ES-SCLC): A Survival, Epidemiology and End Results (SEER) Analysis. Int J Radiat Oncol Biol Phys. 2017; 99(2): E495, doi: 10.1016/j.ijrobp.2017.06.1785.

9. Lutz S, Balboni T, Jones J, et al. Palliative radiation therapy for bone metastases: Update of an ASTRO Evidence-Based Guideline. Pract Radiat Oncol. 2017; 7(1): 4–12, doi: 10.1016/j.prro.2016.08.001, indexed in Pubmed: 27663933.
10. De Felice F, Piccioli A, Musio D, et al. The role of radiation therapy in bone metastases management. Oncotarget. 2017; 8(15): 25691–25699, doi: 10.18632/oncotarget.14823, indexed in Pubmed: 28148890.
11. Cox JD, Stetz J, Pajak TF. Toxicity criteria of the Radiation Therapy Oncology Group (RTOG) and the European Organization for Research and Treatment of Cancer (EORTC). Int J Radiat Oncol Biol Phys. 1995; 31(5): 1341–1346, doi: 10.1016/0360-3016(95)00060-C, indexed in Pubmed: 7713792.
12. Riihimäki M, Hemminki A, Fallah M, et al. Metastatic sites and survival in lung cancer. Lung Cancer. 2014; 86(1): 78–84, doi: 10.1016/j.lungcan.2014.07.020, indexed in Pubmed: 25130083.
13. Kawano D, Takeo S, Katsura M, et al. Surgical treatment of stage IV non-small cell lung cancer. Interact Cardiovasc Thorac Surg. 2012; 14(2): 167–170, doi: 10.1093/icvts/ivr036, indexed in Pubmed: 22159239.
14. Li J, Zhu H, Sun L, et al. Prognostic value of site-specific metastases in lung cancer: A population based study. J Cancer. 2019; 10(14): 3079–3086, doi: 10.7150/jca.30463, indexed in Pubmed: 31289577.
15. Janssen S, Kaesmann L, Schild SE, et al. Impact of the Radiation Dose and Completion of Palliative Radiotherapy on Survival in Patients Treated for Locally Advanced Lung Cancer. Anticancer Res. 2016; 36(4): 1825–1828, indexed in Pubmed: 27069165.
16. Støchkel Frank M, Schou Nørøxe D, Nygård L, et al. When is referral of Heaf test positive schoolchildren worth while? Prospective study. BMJ. 1996; 313(7059): 726–727, doi: 10.1136/bmj.313.7059.726, indexed in Pubmed: 8819443.
17. Westhoff PG, de Graeff A, Monninkhof EM, et al. Dutch Bone Metastasis Study Group. Effectiveness and toxicity of conventional radiotherapy treatment for painful spinal metastases: a detailed course of side effects after opposing fields versus a single posterior field technique. J Radiat Oncol. 2018; 7(1): 17–26, doi: 10.1007/s13566-017-0328-1, indexed in Pubmed: 29576859.
18. Brown PD, Ahluwalia MS, Khan OH, et al. Whole-Brain Radiotherapy for Brain Metastases: Evolution or Revolution? J Clin Oncol. 2018; 36(5): 483–491, doi: 10.1200/JCO.2017.75.9589, indexed in Pubmed: 29272161.
19. Nieder C, Tollali T, Yobuta R, et al. Palliative Thoracic Radiotherapy for Lung Cancer: What Is the Impact of Total Radiation Dose on Survival? J Clin Med Res. 2017; 9(6): 482–487, doi: 10.14740/jocmr2980w, indexed in Pubmed: 28496548.
20. Moeller B, Balagamwala EH, Chen A, et al. Palliative thoracic radiation therapy for non-small cell lung cancer: 2018 Update of an American Society for Radiation Oncology (ASTRO) Evidence-Based Guideline. Pract Radiat Oncol. 2018; 8(4): 245–250, doi: 10.1016/j.prro.2018.02.009, indexed in Pubmed: 29625898.
21. Mok TS, Wu YL, Thongprasert S, et al. Gefitinib or carboplatin-paclitaxel in pulmonary adenocarcinoma. N Engl J Med. 2009; 361(10): 947–957, doi: 10.1056/NEJMoa0810699, indexed in Pubmed: 19692680.
22. Rosell R, Carcereny E, Gervais R, et al. Spanish Lung Cancer Group in collaboration with Groupe Français de Pneumo-Cancérologie and Associazione Italiana Oncologia Toracica. Erlotinib versus standard chemotherapy as first-line treatment for European patients with advanced EGFR mutation-positive non-small-cell lung cancer (EURTAC): a multicentre, open-label, randomised phase 3 trial. Lancet Oncol. 2012; 13(3): 239–246, doi: 10.1016/S1470-2045(11)70393-X, indexed in Pubmed: 22285168.
23. Shaw AT, Kim DW, Nakagawa K, et al. Crizotinib versus chemotherapy in advanced ALK-positive lung cancer. N Engl J Med. 2013; 368(25): 2385–2394, doi: 10.1056/NEJMoa1214886, indexed in Pubmed: 23724913.
24. Solomon BJ, Mok T, Kim DW, et al. PROFILE 1014 Investigators. First-line crizotinib versus chemotherapy in ALK-positive lung cancer. N Engl J Med. 2014; 371(23): 2167–2177, doi: 10.1056/NEJMoa1408440, indexed in Pubmed: 25470694.
25. Shaw AT, Ou SHI, Bang YJ, et al. Crizotinib in ROS1-rearranged non-small-cell lung cancer. N Engl J Med. 2014; 371(21): 1963–1971, doi: 10.1056/NEJMoa1406766, indexed in Pubmed: 25264305.
26. Mazières J, Zalcman G, Crinò L, et al. Crizotinib therapy for advanced lung adenocarcinoma and a ROS1 rearrangement: results from the EUROS1 cohort. J Clin Oncol. 2015; 33(9): 992–999, doi: 10.1200/JCO.2014.58.3302, indexed in Pubmed: 25667280.
27. Herbst RS, Baas P, Kim DW, et al. Pembrolizumab versus docetaxel for previously treated, PD-L1-positive, advanced non-small-cell lung cancer (KEYNOTE-010): a randomised controlled trial. Lancet. 2016; 387(10027): 1540–1550, doi: 10.1016/S0140-6736(15)01281-7, indexed in Pubmed: 26712084.
28. Rittmeyer A, Barlesi F, Waterkamp D, et al. OAK Study Group. Atezolizumab versus docetaxel in patients with previously treated non-small-cell lung cancer (OAK): a phase 3, open-label, multicentre randomised controlled trial. Lancet. 2017; 389(10066): 255–265, doi: 10.1016/S0140-6736(16)32517-X, indexed in Pubmed: 27979383.