International Journal of Academic Health and Medical Research (IJAHMR)
ISSN: 2643-9824
Vol. 8 Issue 5 May - 2024, Pages: 30-36

Predictive factors for survival of lung cancer patients after radiotherapy

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Abstract: Background*: Lung cancer remains one of the leading causes of cancer-related death worldwide, particularly in advanced stages, underscoring the importance of effective treatment strategies. Radiotherapy plays a crucial role in the treatment of lung cancer, either alone or in combination with other modalities. The aim of our work is to identify predictive factors for survival after radiotherapy, which is essential to optimize patient outcomes.* ***Methods****: We conducted a 5-year retrospective cohort study at the Tangier Oncology Center, including patients diagnosed with lung cancer who underwent radiotherapy.* ***Results****: Ninety-seven patients were included, with a male/female sex ratio of 7.81 and a mean age of 59.8 years (± 9.2). Univariate analysis revealed associations indicating that smoking, disease progression, and type of palliative radiotherapy were associated with poor prognosis, whereas type of curative radiotherapy and high dose radiation were associated with good prognosis. Multivariate analysis confirmed that smoking was associated with an unfavorable outcome (OR: 4.73, 95% CI: 1.15-19.46, p < 0.031), whereas curative radiotherapy was associated with a favorable outcome (OR: 0.22, 95% CI: 0.06-0.75, p < 0.016). In the five-year survival analysis, we found a survival probability of 30.6% among patients, with a median survival time of 16 months (95% CI: [5.44 - 26.55].* ***Conclusion****: In conclusion, our findings underscore the multifaceted nature of lung cancer prognosis and response to treatment after radiotherapy. The association between smoking and adverse outcomes highlights the critical importance of smoking cessation interventions in lung cancer management. Conversely, the favorable prognosis associated with curative radiotherapy emphasizes the importance of aggressive treatment approaches.*

Keywords— Lung cancer, Radiotherapy, Survival, Predictive factors, Smoking.

1. INTRODUCTION

Lung cancer ranks among the leading causes of cancer-related deaths worldwide [1–4], with a notably poor prognosis, especially in advanced stages [5,6]. Despite advancements in treatment modalities, including surgery, chemotherapy, targeted therapy, and immunotherapy, the management of lung cancer remains challenging [7–9]. Radiotherapy plays a crucial role in the treatment paradigm, either as a standalone therapy or in combination with other modalities [10–12]. Understanding predictive factors for survival post-radiotherapy is essential for optimizing treatment strategies and improving patient outcomes [13,14].

Prognostic factors in lung cancer play a crucial role in determining the disease process and selecting treatment options [15]. Several factors are associated with a favorable or unfavorable prognosis in lung cancer patients [14–16]. Among the most widely studied prognostic factors are the stage of the disease at diagnosis [17], the presence of metastases, the histological type of cancer (small-cell or non-small-cell), the patient's general state of health, and characteristics such as age and sex [5,16]. In addition, factors such as smoking status and response to initial treatment can also influence prognosis [13]. Studies have shown that smoking is associated with a less favorable prognosis in lung cancer, due to its impact on disease progression and response to treatment [18–20]. In our Moroccan population, there are few published studies in this regard, so we aim to shed light on this subject and identify the prognostic factors for survival post radiotherapy associated with lung cancer in our population. By taking these factors into account, clinicians can better assess each patient's prognosis and adapt treatment strategies to improve clinical outcomes.

2. METHODS:

We conducted a retrospective cohort study over a 5-year period, from 2018 to 2022, of patients diagnosed with lung cancer of any histological type and treated with radiotherapy in our oncology center. Inclusion criteria included all patients diagnosed with lung cancer who were subsequently treated with radiotherapy at our facility. Exclusion criteria were applied to files in which essential data on treatment modality, disease stage and survival outcomes were missing.

Data collected included patient demographics, tumor characteristics, tumor staging specifics, therapeutic approaches, and survival outcomes. Statistical analyses were performed using IBM SPSS v21, including descriptive analyses represented by percentages and means, as well as assessments of five-year overall survival. Univariate analysis was performed to identify the association between final disease outcome and prognostic factors, and Multivariate analysis was performed to address the founding factors. A significance level of $p<0.05$ was adopted.

3. RESULTS

3.1 DESCRIPTIVE SAMPLE DATA

Ninety-seven patients were included in the study, with a male-to-female sex ratio of 7.81. The majority of patients presented respiratory symptoms, including chest pain (58.1%), dyspnea (62.8%), hemoptysis (32.6%), emphysema (46.5%), BCPO (20.9%), superior vena cava syndrome (33.3%), and bronchial dilatation (6.1%).

The most predominant histological type in our study is the Non-small cell lung cancer (NSCLC) accounting for 89.4%, followed by Small cell lung cancer (SCLC) at 10.6%.

Regarding the treatment received by patients, concomitant chemotherapy was the preferred treatment with a percentage of 95.2% using the 3D technique for radiotherapy in all patients (**Table 1**).

Table 1. Patient characteristics:

Variables	**n (Percentage %) (n=97)**
Age, Mean (SD)	59.8 (+/- 9.2)
Pack of smoking years, Mean (SD)	20 (+/-12)
Total radiotherapy dose; Mean (SD)	34.8(+/-22)
Sex, n (%)	
Male	86 (88.7)
Female	11 (11.3)
Comorbidity	
Yes	40 (44.6)
No	49 (50.5)
Smoking status	
Yes	54 (55.7)
No	43 (44.3)
Alcohol	
Yes	12 (27.9)
No	31 (72.1)
Treatment received	
Chemotherapy	80 (95.2)
Radiotherapy	97 (100)
Disease progression	
Yes	77 (79.4)
No	20 (20.6)
Metastasis localization	
Brain metastasis	41 (65.1)
Bone metastasis	13 (20.6)
Another site	09 (14.3)
Type of radiotherapy	
Curative	34 (35.1)
Palliative	63 (64.9)
Final outcome	
Decease	48 (49.5)
Lost sight	28 (28.9)
Follow-up stable	21 (21.6)

3.2 PROGNOSTIC FACTORS OF LUNG CANCER POST RADIOTHERAPY TREATMENT

In the univariate analysis, we examined the association between prognostic factors and final outcome (Death/No post-treatment death) (**Table 2**).

Our results suggest that smoking is associated with a worse prognosis, along with disease progression and the specific approach to palliative radiotherapy.

In summary, the use of palliative treatments aimed at symptom management rather than cure is associated with a poor prognosis, whereas curative treatments above 56 Gray are associated with a better prognosis.

Table 2: Factors associated with the final outcome of patients with lung cancer.

Factors	Death	No post treatment death	p-value
Sex			0.427
Male	67.7%	32.3%	
Female	85.7%	14.3%	
Comorbidity			0.338
Yes	76.7%	23.3%	
No	65.6%	34.4%	
Smoking			**<0.002**
Yes	89.7%	10.3%	
No	55%	45%	
Pack of smoking years			
≤ 30 years	36.4%	63.6%	0.163
> 30 years	100%	0%	
Histologic type*			0.257
NSCLC	82.9%	17.1%	
SCLC	60%	40%	
Disease progression			**<0.027**
Yes	75.9%	24.1%	
No	36.4%	63.6%	
Metastasis localization			0.311
Brain	85.3%	14.7%	
Bone	85.7%	14.3%	
Another site	62.5%	37.5%	
Type of radiotherapy			**<0.001**
Curative	40%	60%	
Palliative	81.6%	18.4%	
Radiotherapy dose			**<0.003**
<56 Gray	79.6%	20.4%	
≥ 56 Gray	42.1%	57.9%	

* NSCLC: Non-small cell lung cancer, SCLC: Small cell lung cancer

To eliminate factors that might affect the results, i.e. confounders, we completed the analysis with a multivariate analysis.

In the initial model, we included significant associations related to the variable of interest, as well as those with a p-value of 0.2 or less. The model includes several variables, such as age, gender, comorbidities, smoking patterns, cumulative pack-years of smoking, type of radiotherapy, disease progression, and the dosage of radiotherapy administered to the patient. The final model's findings reveal two significant associations: one between smoking habits and final outcome, and the other between the type of radiotherapy and final outcome. The study found that smoking is a prognostic factor for an unfavorable final outcome, with an odds ratio (OR) of 4.73 [95% CI: 1.15-19.46], $p < 0.031$, while curative radiotherapy is a prognostic factor for a favorable final outcome, with an OR of 0.22 [95% CI: 0.06-0.75], $p < 0.016$ (**Table3**).

Table 3: Final model of the multivariate analysis

Prognostic factors	OR (95% CI)	p=value
Smoking		
Yes	4.73[1.15-19.46]	<0.031
No	-	
Type of radiotherapy		
Curative	0.22[0.06-0.75]	<0.016
Palliative	-	

3.3 Analysis of overall survival in our population of patients with lung cancer

In our five-year survival analysis of lung cancer patients, we found that 30.6% of patients were still alive five years after initial diagnosis. This means that of the 100 patients included in our study, 30.6 survived to the end of the five-year follow-up period, with a median survival time of 16 months [95% CI: 5.44 - 26.55] (**Figure 1**).

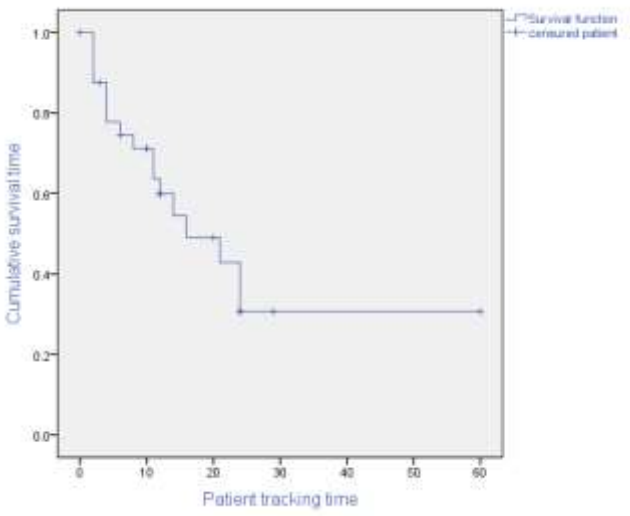

Figure 1*: Overall survival curve at 5 years for lung cancer patients followed in our oncology center.*

4. DISCUSSION

Our study seeks to identify factors predictive of survival in lung cancer patients. Through our results highlight several notable associations between smoking status, curative treatment, disease progression, and survival outcome.

First, our univariate analysis revealed a significant association between smoking and adverse outcomes. This finding is consistent with extensive literature highlighting the deleterious effects of tobacco on lung health and the increased risk of lung cancer development and progression as explained by Zhou et al in their study [21]. The carcinogens in tobacco smoke cause extensive damage to lung tissue, promote oncogenic transformation and facilitate disease progression [22–25]. In addition, tobacco use is often associated with other unhealthy lifestyle behaviors, exacerbating the overall impact on patient health and prognosis [26].

Secondly, our analysis also highlighted the importance of radiotherapy curative treatment for patient survival. We found that patients who received curative treatment had a good prognosis compared to patients who received palliative care, which aims only to relieve symptoms, improve quality of life and provide holistic support for patients with advanced lung cancer [27]. Curative radiotherapy treatment is associated with early stages of cancer, which is linked to the curative dose of radiation delivered [28], This explains the results observed in the analysis: a dose exceeding 56 Gray is significantly associated with a favorable prognosis. These findings align with the existing literature, as indicated in the critical review by Baker et al [29].

In addition, our study reveals a highly significant association between disease progression and poor prognosis, which is explained by the dynamic nature of lung cancer, reflected in the continuous progression of malignant cells, resulting in worsening symptoms, deterioration of organ function and, ultimately, reduced survival [30,31].

Although our study examined several factors, including sex, age, and histologic subtype, we did not find significant associations between these variables and the final outcome in our analysis. This suggests that within the scope of our study population and methodology, these factors may not exert a substantial independent influence on patient survival in lung cancer [32].

Sex, although recognized as a potential determinant of cancer incidence and outcome in certain contexts [25,33–36], did not emerge as a significant predictor of final outcome in our study. Similarly, age did not demonstrate a significant independent impact on survival in our analysis, despite its known association with increased cancer risk and in some cases disease invasiveness [32], and according to the predictions of the CISNET model, the predictions increase as people get older, quit smoking later, or smoke more heavily. Conversely, starting smoking at an older age leads to lower predictions [37].

In addition, histologic classification, which includes; Non-small cell lung cancer (NSCLC) and Small cell lung cancer (SCLC), did not show a significant association with final outcomes in our study. While histologic classification plays a critical role in guiding treatment decisions and prognostic assessments in lung cancer, our results suggest that within the parameters of our analysis, histologic type alone may not be a robust predictor of survival independent of other factors [38,39].

Although these factors did not appear to be significant independent predictors of final outcome in our study, it is important to recognize that their influence on patient prognosis may vary depending on numerous contextual factors, including tumor stage, molecular characteristics, early diagnosis, and others [40–42].

The results of the multivariate analysis confirmed the negative impact of smoking on patient outcomes, even when other covariates were considered. Smoking emerged as a significant independent predictor of adverse outcomes, demonstrating its pervasive and detrimental influence on lung cancer prognosis.

On the other hand, our multivariate analysis also highlighted the beneficial role of curative dose radiotherapy in patient outcome. These findings underscore the critical importance of early, aggressive intervention to eradicate or control disease burden, thereby increasing the likelihood of long-term survival and disease-free remission [43].

Finally, our analysis revealed an overall survival rate of 30.6%, with a median survival time of 16 months underscoring the enormous challenge of lung cancer and the unfortunate reality faced by many patients diagnosed with this

malignancy. These results are comparable to the predictive models based on machine learning applied by Lynch et al, which showed a median survival of 15.30 months [44]. Others studies showed similar results of overall survival time [45,46]. Despite advances in diagnostic modalities and therapeutic interventions, lung cancer remains a challenging adversary characterized by high mortality rates and limited treatment options, particularly in advanced stages [47]. Poor overall survival underscores the urgent need to continue research efforts aimed at unraveling the complexities of lung cancer biology, identifying novel therapeutic targets and developing innovative treatment modalities to improve patient outcomes and survival [7,8].

Several predictive factors influencing survival in lung cancer patient's post-radiotherapy were identified [9,15,48]. The contrasting roles of tobacco consumption and curative treatment in influencing patient outcomes underscore the critical importance of targeted interventions and personalized treatment approaches in lung cancer management [49–51]. While tobacco cessation initiatives are essential for reducing disease risk and improving overall health outcomes [52], the provision of timely and appropriate curative treatments is equally crucial for optimizing survival and quality of life in affected individuals [7,10]. By addressing both modifiable risk factors and therapeutic interventions, clinicians can adopt a comprehensive and patient-centered approach to lung cancer care, thereby maximizing the likelihood of favorable outcomes and improved survival rates [8,53]. Further research is warranted to validate these predictive factors and explore additional factors that may enhance prognostic accuracy in lung cancer patients undergoing radiotherapy.

Our study has several limitations. First, our reliance on medical records introduces the risk of incomplete or inaccurate documentation, potentially leading to biased results or missing important details relevant to our study objectives. In addition, the retrospective nature of our study inherently limits our control over variables and may not adequately capture the complexity of patient experience or disease progression, beside these limitations we had a relatively small sample size of approximately 97 patients. However, despite these limitations, our study is promising, particularly in examining predictive factors of survival in lung cancer, a relatively understudied area. By exploring this important issue, our study has the potential to provide new insights into this critical aspect of patient care, identify previously unrecognized prognostic indicators, and contribute to the advancement of medical knowledge. Future research efforts may benefit from examining these factors in more detail in larger sample sizes and elucidating their interplay with other variables to gain a more comprehensive understanding of their impact on lung cancer outcomes.

Conclusion:

In conclusion, our findings underscore the multifaceted nature of lung cancer prognosis and response to treatment after radiotherapy. The association between smoking and adverse outcomes highlights the critical importance of smoking cessation interventions in lung cancer management. Conversely, the favorable prognosis associated with curative radiotherapy emphasizes the importance of aggressive treatment approaches.

Our study provides valuable insights into predictive factors for survival after radiotherapy, guiding clinicians in optimizing treatment strategies and improving patient outcomes. Moving forward, continued research efforts are essential to validate and refine these findings and ultimately advance the field of lung cancer treatment.

By tailoring treatment approaches based on identified prognostic factors, we can strive to improve survival and quality of life for people living with lung cancer. Together, these efforts offer hope for improved outcomes and better support for patients facing this challenging disease.

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