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Covid-19 and lung cancer: A greater fatality rate?

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ABSTRACT

Background: Currently there are no reported series determining the Covid-19 infected lung cancer patient´s characteristics and outcome that allow us to clarify strategies to protect our patients.

In our study we determine whether exists differences in cumulative incidence and severity of Covid-19 infection between lung cancer patients visiting our Medical Oncology department and the reference population of our center (320,000 people), in the current epicenter of the pandemic in Europe (Madrid, Spain). We also describe clinical and demographic factors associated with poor prognosis and Covid-19 treatment outcomes.

Patients and methods: We retrospectively reviewed 1878 medical records of all Covid-19 patients who were admitted at Hospital Universitario Infanta Leonor of Madrid between March 5, 2020 and April 7, 2020, in order to detect cumulative incidence of Covid-19 in lung cancer patients.

We also described Covid-19 treatment outcome, mortality and associated risk factors using univariate and multivariate logistic regression analysis.

Results: 17/1878 total diagnosis in our center had lung cancer (0.9 %) versus 1878/320,000 of the total reference population ($p = 0.09$). 9/17 lung cancer patients with Covid-19 diagnosis died (52.3 %) versus 192/1878 Covid-19 patients in our center ($p < 0.0001$). Dead lung cancer patients were elderly compared to survivors: 72 versus 64.5 years old ($p = 0.12$). Combined treatment with hydroxychloroquine and azithromycin improves the outcome of Covid-19 in lung cancer patients, detecting only 1/6 deaths between patients under this treatment versus others treatment, with statistical significance in the univariate and multivariate logistic regression (OR 0.04, $p = 0.018$).

Conclusions: Lung cancer patients have a higher mortality rate than general population. Combined hydroxychloroquine and azithromycin treatment seems like a good treatment option. It is important to try to minimize visits to hospitals (without removing their active treatments) in order to decrease nosocomial transmission.

1. Introduction

In December 2019, multiple cases of atypical pneumonia of unknown origin were detected in China. At the same time, a new coronavirus subtype was discovered as the etiology behind these described cases in Wuhan, Hubei (China). This novel microorganism detected, called as severe acute respiratory syndrome coronavirus 2 (SARS−COV-2), has an enormous virulence and a high human-to-human transmission capacity [1,2]. Thanks to its virulence, the SARS−COV-2 has been able to spread throughout the world, creating the unprecedented pandemic in which we are involved. Although the new coronavirus has a high human-to-human capacity transmission, it had a lower mortality than other previously isolated coronaviruses [3]. However, the virus is capable of developing serious bilateral pneumonias and worrying inflammatory responses [4].

On January 31, 2020, the first case of coronavirus was detected in Spain, in La Gomera Island. However, it was not until February 25, 2020, when the first case took place in Madrid, the most active focus currently in Europe. A few days after the detection of the first case in Madrid, the health alert was declared, detecting an intracommunity transmission in Spain. In those moments, the infectious outbreak was classified as a pandemic by the world health organization (WHO) due to its extension. This unprecedented fact has changed the activity of the hospitals focusing on the diagnosis and treatment of the patients with

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Covid-19.

Cancer patients are at increased risk of Covid-19 infection. These patients must maintain their visits to Oncology departments. They should continue receiving their diagnoses and treatments to avoid complications from their own oncological pathology [5].

In some reports, it has been described that the risk-benefit should be assessed in the planning of visits and treatments in cancer patients [6] as well as in patients with only lung cancer diagnosis, trying to make as few visits as possible [7].

In a study carried out by Yu J. in China, they described how patients with non-small cell lung cancer (NSCLC) have a higher incidence and severity of Covid-19 [8]. However, in other studies, they described an increase in the cumulative incidence of Covid-19 in all cancer population. They did not describe a greater severity in patients with lung cancer [9,10].

In our study, we determine whether exists differences in cumulative incidence and severity of Covid-19 infection between lung cancer patients visiting our Medical Oncology department and the reference population of our center (320,000 people), in the current epicenter of the pandemic in Europe (Madrid, Spain). We also describe clinical and demographic factors associated with poor prognosis and Covid-19 treatment outcomes.

2. Material and methods

We retrospectively reviewed 1878 medical records of all patients with Covid-19 diagnosis admitted at Hospital Universitario Infanta Leonor of Madrid, since the first Covid-19 diagnosis date, March 5, 2020, to April 7, 2020. We studied cumulative incidence of Covid-19 infection and its mortality in lung cancer patients. Covid-19 diagnosis was made based on WHO criteria and/or confirmed by RT-PCR of nasopharingeal specimens.

Descriptive analyses are reported as relative frequencies for discrete variables. Continuous variables are reported as mean ± standard deviation (SD) or median and interquartile range (IQR) for normal and not normally distributed variables, respectively. To determine differences on mortality between lung cancer patients and general population, Fisher´s Exact Test were performed. To determine the relationship between clinical and demographic risk factors with mortality, Chi square Test, univariate logistic regression and multivariate logistic regression were performed. Statistical analyses were carried out with STATA SE version 14.1 (StataCorp, College Station, TX, USA). A p-value < 0.05 was considered statistically significant.

3. Results

Seventeen cases of lung cancer with Covid-19 infection were detected in our center. The median age was 68 years old (range 49–83). Regarding gender, a higher prevalence of males were detected (n = 13, 76.5 %). Most frequent histology was non-small cell lung cancer (n = 16, 94.1 %). Most affected patients had metastatic disease (n = 11, 64.7 %) and received chemotherapy (n = 5, 29.4 %). Table 1. All patients who were able to receive treatment for Covid-19 infection received hydroxychloroquine (n = 12, 70.6 %), most combined with azithromycin (n = 8, 47.1 %). All patients required admission except for 4 patients (76.5 %), 11 of them being diagnosed with severe Covid-19 infection (64.7 %). None of the patients were admitted to the ICU, either because they did not need it, or because it was not admitted due to their comorbidities. Table 2. About comorbidities, 10 patients had hypertension (51.1 %), 9 patients Chronic Obstructive Pulmonary Disease (COPD) (52.4 %), 3 patients obesity (17.6 %), 2 patients diabetes (11.7 %) and 1 patient chronic kidney disease (5.8 %). Table 1.

Seventeen cases of lung cancer with Covid-19 infection were detected among the 45 cancer patients (37.7 %), which supposes a cumulative incidence of 0.9 % on the total of 1878 infected patients at data cut off versus 0.58 % in our reference population (1878 patients of 320,000 inhabitants, Fisher's exact test, p = 0.09). Regarding mortality, we detected that 9/17 patients (52.3 %) with lung cancer died versus 192 over the total of 1878 Covid-19 patients in our center (Fisher's exact test, $p < 0.0001$). Regarding dead lung cancer patients, two patients were under chemotherapy, two patients under best supportive care, one patient under checkpoint inhibitor treatment (nivolumab), one patient under tyrosine kinase inhibitor (gefitinib), one patient underwent surgery and two patients were new diagnosis.

A trend towards statistical significance was detected in the mean age between the patients with lung cancer who died and those who are still alive: 72 versus 64.5 years old in the survivors' subgroup (p = 0.12). No other associations between mortality and other clinical demographic variables, patient's symptoms or comorbidities were detected.

Combined treatment with hydroxychloroquine and azithromycin

Table 1
Clinical and demographic characteristics of lung cancer patients.

Characteristics	N	Percentage (%)
Sex		
Male	13	23.5
Female	4	76.5
Histologies		
Non-small cell lung cancer	16	94.1
Small cell lung cancer	1	5.9
Cancer staging		
Localizated	3	17.7
Locally advanced	3	17.7
Metastatic	11	64.6
Cancer treatment		
Best supportive care	6	35.3
Chemotherapy	5	29.5
TKIs	2	11.7
New diagnosis	2	11.7
Immunotherapy	1	5.9
Surgery	1	5.9
Comorbidities		
Hypertension	10	58.8
Diabetes Mellitus	2	11.7
Chronic kidney disease	1	5.9
COPD	9	52.9
Obesity	3	17.6

*Abbreviations: TKIs: Tyrosine kinase Inhibitors. COPD: Chronic obstructive pulmonary disease.

Table 2
Management, outcome, symptoms and treatment of Covid-19 lung cancer patients.

	N	Percentage (%)
Covid-19 diagnosis		
Hospitalization admission	13	76.4
ICU admission	0	0
Home management (discharged from hospital at diagnosis)	4	23.5
Covid-19 outcome		
Dead	9	52.9
Alive	8	47.1
Severe covid-19 infection	11	64.7
Symptoms		
Fever	12	70.6
Cough	17	100
Myalgia	5	29.4
Dyspnea	13	76.4
Diarrhea	1	5.9
Covid-19 treatment		
Lopinavir/ritonavir + Hydroxichloroquine	2	11.7
Hydroxichloroquine + azithromycin	8	47.1
Lopinavir/ritonavir + Hydroxichloroquine + azithromycin	1	5.9
Hydroxichloroquine	1	5.9

Table 3
Clinical and demographic parameters in both subgroup of lung cancer patients (dead patients or survivors).

	Survivor patients (N = 8)	Dead patients (N = 9)	*p* value
Age, median	72	64.5	0.12
Male, n (%)	7 (87.5)	6 (66.7)	0.31
Cancer characteristics			
Cancer treatment			
Chemotherapy, n (%)	3 (37.5 %)	2 (22.2 %)	0.70
Staging			
Metastatic disease, n (%)	4 (50.0 %)	7 (77.8 %)	0.23
Covid-19 characteristics			
Covid-19 Treatment			
Hydroxichloroquine + azytromicin, n (%)	7 (87.5 %)	1 (11.1 %)	003
Covid-19 symptoms			
Fever, n (%)	6 (75.0 %)	6 (66.7 %)	0.70
Cough, n (%)	8 (100 %)	9 (100 %)	–
Severe infection, n (%)	4 (50.0 %)	7 (77.8 %)	023
Comorbidities			
Hypertension, n (%)	4 (50.0 %)	6 (66.7 %)	0.48
COPD, n (%)	5 (62.5 %)	4 (44.4 %)	0.45
CKD, n (%)	1 (12.5 %)	0 (0.0 %)	0.27
Obesity, n (%)	1 (12.5 %)	2 (22. %)	0.60

Abbreviations: COPD: chronic obstructive pulmonary disease; CKD: chronic kidney disease.

improves the outcome of Covid-19 lung cancer patients, detecting only 1/8 deaths between patients under this treatment (OR 0.04, CI 0.01 − 0.57, p = 0.018). Table 3. Similar results were observed in the multivariate logistic regression adjusted by age (OR 0.02, CI 0.001 − 0.588, p = 0.02).

4. Discussion

In our study, a significant increase in mortality rate in lung cancer patients with Covid-19 was detected compared to all Covid-19 patients in our center. Considering the characteristics of the lung cancer patients, with a greater predisposition to respiratory infections, immunosuppressed patients, and most of them with a previous diagnosis of COPD and metastatic disease, we expected to observe greater mortality or, at least, greater severity of the infectious symptoms.

In three Chinese series performed with heterogeneous samples of cancer patients, they described that the most frequent type of tumor in their series was lung cancer [8–10]. However, only one of them described a higher susceptibility and severity for Covid-19 in NSCLC [9]. In the other two remaining studies, they indicated that this population is the most frequently infected as we previously have indicated [9,9,10]. Nevertheless in the study by Liang W did not find that lung cancer patients had a higher risk of complications compared to the rest of the oncology population from their work [9]. These results are likely to be found in this study because most of its patients were cancer survivors.

In our study, most of the lung cancer patients had active disease or were on active treatment. This is why we probably obtained a higher mortality rate, being more representative of the real world in oncology departments. Refusal to ICU admission could also act as a determining factor. These data are similar to those recently reported by Garassino MC [11]. They observed a lower mortality rate (33.3 %), but they also agree that a determining fact in these deaths, was the refusal to ICU admission. These considerations will guide us to make better recommendations.

Furthermore, none of these three published studies [9–11] provide specific data on Covid-19 treatment outcome. In our study, we have checked in the multivariate analysis that hydroxychloroquine and azithromycin combination may be a good treatment option in patients with lung cancer with just one dead patient, but we cannot draw conclusions due to the limited number of cases of our study.

To our knowledge, this is the one of the only homogeneous case series of lung cancer and Covid-19, and with many more lung cancer patients included than the individual analyses performed within the heterogeneous Chinese series, only being overtaken by preliminary data reported from Teravolt study [11]. Our work is the only one that provides data in lung cancer outcome to Covid-19 treatment. However, there are some limitations: our study is a retrospective review, and despite being one of the largest ones focused on a single subtype of cancer, it still has a limited and heterogeneous number of patients.

5. Conclusion

Lung cancer patients have a higher mortality rate than general population, with 52.3 % of dead patients in our series. Due to the high lethality in this subgroup of cancer patients, it is important to try to minimize visits to hospitals (without removing their active treatments) in order to decrease nosocomial transmission.

Authors contributions

J.R. contributed to the conception and design of the study, data acquisition, statistical analysis, interpretation of the data and writing of the manuscript. C.P and G.S.M contributed to the conception and design of the study, interpretation of the data and writing of the manuscript. B.O., A.M.M., M.P.P., A.L.A. contributed to the acquisition of the data. P.G. contributed to the statistical analysis and interpretation of the data. M.A.L. contributed to the conception and design of the study, interpretation of the data and writing of the manuscript. All authors reviewed and approved the final version of the manuscript.

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Declaration of Competing Interest

The authors declare no conflict of interest for the present work.

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References

[1] C. Wang, P.W. Horby, F.G. Hayden, et al., A novel coronavirus outbreak of global health concern, Lancet S0140-6736 (20) (2020) 30185–30189 published online Jan 24.
[2] Q. Li, X. Guan, P. Wu, et al., Early Transmission Dynamics In Wuhan, China, of Novel Coronavirus-Infected PneumoniaEarly transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia, N. Engl. J. Med. 382 (2020) 1199–1207.
[3] Y. Yin, Wunderink RG. MERS, SARS and other coronaviruses as causes of pneumonia, Respirology 23 (2) (2018) 130–137.
[4] P. Conti, G. Ronconi, A. Caraffa, et al., Induction of pro-inflammatory cytokines (IL-1 and IL-6) and lung inflammation by Coronavirus-19 (COVI-19 or SARS-CoV-2): anti-inflammatory strategies, J. Biol. Regul. Homeost. Agents 34 (2) (2020) March 14.
[5] F. Cortiula, A. Pettke, M. Bastoletti, et al., Managing COVID-19 in the oncology clinic and avoiding the distraction effect, Ann. Oncol. (March 19) (2020).
[6] P. Sidaway, COVID-19 and cancer: what we know so far, Nat. Rev. Clin. Oncol. (2020).
[7] G. Banna, A. Curioni-Fontecedro, A. Friedlaender, et al., How we treat patients with lung cancer during the SARS-CoV-2 pandemic: primum non nocere, ESMO Open 5 (2020) e000765.
[8] J. Yu, W. Ouyang, M.L.K. Chua, et al., SARS-CoV-2 transmission in patients with Cancer at a tertiary care hospital in Wuhan, China, JAMA Oncol. (March 25) (2020) Published Online.
[9] W. Liang, W. Guan, R. Chen, et al., Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China, Lancet Oncol. S1470-2040 (20) (2020) Published

online February 14 30096-6.
[10] L. Zhang, F. Zhu, C. Xie, et al., Clinical characteristics of COVID-19-infected cancer patients: a retrospective case study in three hospitals within Wuhan, China, Ann. Oncol. S0923-7534 (20) (2020) 36383.
[11] M.C. Garassino, TERAVOLT (thoracic cancER interational coVid 19 cOLlaboraTion): first results of a global collaboration to address the impact of COVID-19 in patients with thoracic malignancies, Abstract. American Association for Cancer Research Virtual Annual Meeting I, April 27-28, 2020.