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Impact of the COVID-19 pandemic on lung cancer diagnosis in the region of Marrakech-Safi, Morocco

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Abstract

Background: The dreadful consequences of the COVID-19 pandemic put an unprecedented pressure on health-care services in Morocco. Lung cancer (LC) patients represent a vulnerable population highly affected by the pandemic. Studies on lung cancer diagnosis during an epidemic are lacking. We analyzed the impact of COVID-19 on lung cancer diagnosis in the region of Marrakech-Safi where lung cancer incidence continues to rise.

Materials and Methods: We compared the clinical features of newly diagnosed lung cancer cases in the Mohammed VI University Hospital Center between March and December 2020 with lung cancer cases diagnosed during the same period in the past 3 years and the year after.

Results: A total of 352 patients were diagnosed with lung cancer from March through December, 2017–2021. During the pandemic, the number of lung cancer hospitalization dropped by 36% from the previous years, moreover the number of bronchoscopies and other biopsies performed decreased significantly in 2020 ($p < 0.000$).Lung cancer patients in Group2 had a significant longer pre-hospital delay with a mean of 7, 02±2,06 months and higher performance status score 3-4 (64,6%) compared to the other Groups 1,3 ($p < 0.000$).In the second and third groups more lung cancer patients seems to be exposed to second-hand smoke comparing to the first group with (27,4%) in 2017-2019 vs (52,1%) and (69,2%) in 2020 and 2021 respectively($p < 0.000$). However no differences concerning tumor staging has been described between the 3 groups with most patients being classified as stage IVA-IVB through all the years (2017-2019: 73,9% vs. 2020: 85,4% vs 2021: 80,8%, p=0,151).

Conclusion: The COVID-19 pandemic was responsible of a significant decrease in newly diagnosed LC cases with less bronchoscopies and biopsies being performed. No significant difference has been noted regarding tumor staging but LC patients seemed to have higher performance status score in 2020.

Keywords: COVID-19; Lung cancer; Oncology; Diagnosis; Pandemic

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1. Introduction

Ever since the coronavirus disease 2019 (COVID-19) started, it has widely and rapidly spread across the globe. On March 11, 2020, the World Health Organization (WHO) [1] has declared it a global pandemic. The dreadful consequences of this pandemic put an unprecedented pressure on health-care services all around the world including Morocco. To deal with the staggering volume of infected patients who need hospitalization new logistical challenges were imposed to the global health care systems and Morocco was no exception. In order to reduce the spread of the disease in Morocco, consultations and emergency care were initially limited. Furthermore, scheduled surgical procedures, including various oncological procedures were temporary suspended in public hospitals across the country. Compared with the previous year, additional deaths not associated with the virus have been reported since the pandemic, suggesting that patients with chronic and severe acute diseases were restricted from healthcare services [2].Subsequently undiagnosed cancer diseases are expected to emerge at a more advanced stage and with a worst prognosis [3]. In addition to that due to the pandemic's repercussions treatment delay or interruption can be detrimental to cancer patient's outcome [4]. Having the highest morbidity and mortality rates among cancers worldwide, lung cancer remains a threat to human health [5]. Although there have been some studies across the world evaluating the global impact of the COVID-19 pandemic on lung cancer management, a lot of work has to be done especially in the African continent where more studies of this nature need to be conducted. This pilot study aimed to appropriately identify and assess the major impact of the COVID-19 pandemic on lung cancer diagnosis in Marrakech, providing new data that could help develop strategy management for chronic diseases during the COVID-19 pandemic and other future epidemics of emerging infectious diseases in Morocco and Africa.

2. Material and methods

2.1. Type, Setting and Period of study

In this single-center retrospective study, we analyzed the data of patients with lung cancer in the Mohammed VI University Hospital Center between March 2017 and December 2021. This hospital is a large regional medical center with 1548 inpatient beds. It is covering the region of Marrakech-Safi, consisting of 7 provinces and a prefecture with nearly 4,520,569 inhabitants representing 13.3% of the national population.

2.2. Study population

After the COVID-19 outbreak, the Moroccan government started a first-level response to public health emergencies on March 20, 2020. The events that followed led to the extension of the state of health emergency months later, subsequently the University Hospital Center's activity didn't fully resume until late December 2020. Therefore, we defined the period of collateral effect of the COVID-19 pandemic from March to December 2020. Newly diagnosed patients with lung cancer during this period were compared with patients diagnosed during the same period in the previous years and the year that followed. Based on their time of diagnosis in relation to the COVID-19 epidemic in Morocco, patients were then divided into 3 groups: Group1: from March to December (2017-2019) ; Group2: from March to December 2020 and Group3:from March to December 2021 . The inclusion criteria were as follows (1): age ≥18 years (2); pathologically confirmed diagnosis, including non-small-cell lung cancer (squamous cell carcinoma and adenocarcinoma) and small-cell lung cancer (3) hospitalization. Exclusion criteria were as follows: (1) recurrent lung cancer (2) pulmonary metastatic disease, (3) presence of lymphoma, thymoma, or other mediastinal tumors; and (4) patients without pathological diagnosis.

2.3. Study design

Between the three Groups we analyzed : clinical characteristics including sex, age, interval time (between the first consultation and pathological diagnosis), number of hospitalizations and duration of hospital stay ; source of diagnosis: interventional diagnostic procedures (percutaneous or surgical lung biopsies, bronchoscopies or other biopsies) related to lung neoplasms ; pathological category; performance status (PS) and finally Lung cancer staging (according to the American Joint Committee on Cancer/International Union Against Cancer 2018 version of lung cancer staging standards)

2.4. Statistical analysis

Statistical analyses were performed with SPSS software, version 16.0 (SPSS Inc., Chicago). Descriptive statistics are presented as counts and proportions for categorical variables and means and standard deviations for continuous variables. Associations between periods and independent factors were assessed using the khi2 test for categorical

variables and T-test for continuous variables. p-value <.05 used to exhibit the suggested statistical difference among parameters.

3. Results

3.1. Demographic characteristics

A total of 535 patients diagnosed with lung cancer had been retrospective analysis but only 352 met our inclusion criteria. Data of 228 lung cancer patients between March and December during 2017–2019, 48 diagnosed during the COVID-19 pandemic between March and December 2020 and 78 patients diagnosed the year after during the same period were analyzed. The mean age of the entire study population was 60,5 ± 9, 5 years with over 51% being above 61 years old (Figure 1).

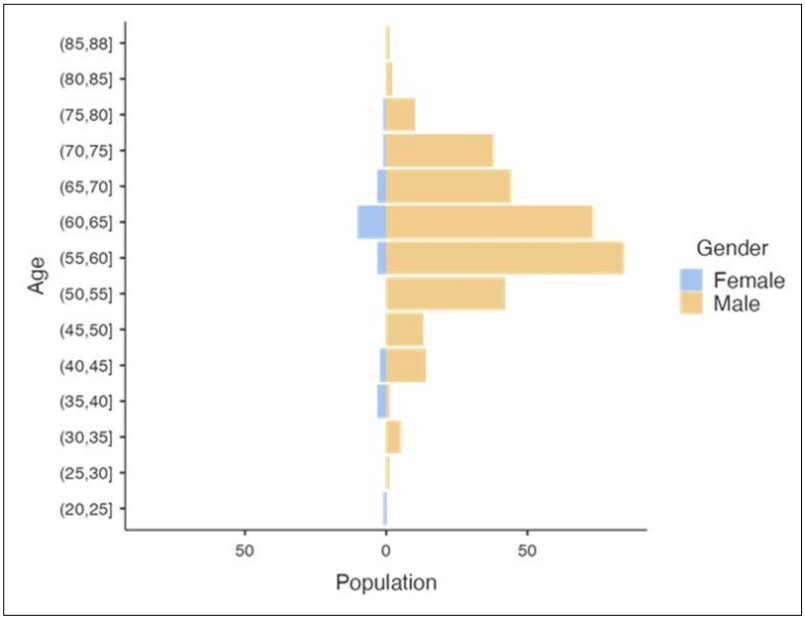

Figure 1 Age and gender distribution in the study population

Majority of the patients were male in (93, 2%) of the cases and (87, 2%) of them were smokers. In the second and third groups more lung cancer patients seems to be exposed to second-hand smoke comparing to the first group with (27,4%) in 2017-2019 vs (52,1%) and (69,2%) in 2020 and 2021 respectively($p < 0.000$).

Table 1 The clinical characteristics of diagnosed lung cancer patients according to diagnoses years

	2017-2019 N (226)	**2020 N(48)**	**2021 N(78)**	**p value**
Age at diagnosis, mean ± SD	60.48± 10.17	60.72± 10,50	60.65± 6.84	p=0.982
Gender (n, %)				
Male	209 (92.5%)	44 (91.7%)	75 (96.2%)	-
Female	17 (7.5%)	4 (8.3%)	3 (3.8%)	-
Smoke (n, %)				
Smoker, ex-smoker	195(86.3%)	43 (89.6%)	69 (88.5%)	p=0,769
Passive smoker	62 (27.4%)	25 (52.1%)	54 (69.2%)	**p < 0.000**
Wood smoke exposure	19 (8.4%)	2 (4.2%)	7(9%)	p=0.185
Pre-hospital delay in months, mean ± SD	2.659± 1.95	7,02±2,06	2,84±1,85	**p < 0.000**

Bronchoscopies per year	204 (90.3%)	25 (52%)	67 (85.9%)	**p < 0.000**
Pathological diagnosis method (n, %)				
Bronchoscopy/ EBUS	138 (61%)	25 (52%)	39 (50%)	p= 0.371
CT-CNB*	70 (31%)	13 (27.1%)	24 (30.8%)	p= 0.865
Pleural biopsy	15 (6.6)	7 (14.6%)	6 (7.7%)	p=0.181
Other biopsies*	29 (12.8%)	3 (1.3%)	9 (11.5%)	**p < 0.000**
Histological subtype (n, %)				
NSCLC	204 (90.3%)	39 (81.3%)	63 (80.8%)	P 0.045
SCLC	22 (9.7%)	9 (18.8%)	15 (19.2%)	
Adenocarcinoma	104 (51%)	15 (38.5%)	28 (44.4%)	-
Squamous	66 (32.4%)	10 (25.6%)	15 (23.8%)	-
Undifferentiated	21 (10.3%)	6 (15.4%)	8 (12.7%)	-
Others	13 (6.4%)	8 (20.5%)	12 (19%)	-
Performance Status, ECOG*				
0-2 (n, %)	128 (57.3%)	17(35.4%)	60 (76.9%)	**p < 0.000**
3-4 (n, %)	96 (42.7%)	31 (64.6%)	18 (23%)	
Final Stage (n, %)				
IIA-IIB	10 (4.4%)	1 (2.1%)	0	p=0.151
IIIA-IIIB-IIIC	49 (21.7%)	6 (12.5%)	15 (19.2%)	
IVA-IVB	167 (73.9%)	41 (85.4%)	63 (80.8%)	

*CT-CNB: Computed tomography-guided cutting needle biopsy; *Lymp nodes biopsy/ skin biopsy / parietal biopsy/ liver biopsy; *ECOG: Eastern Cooperative Oncology Group, NSCLC non-small cell lung cancer, SCLC small cell lung cancer

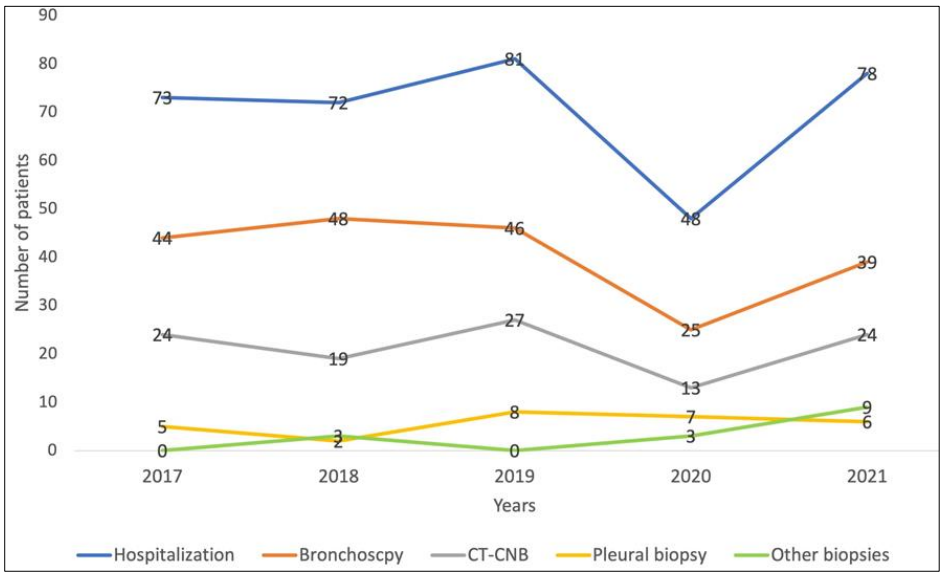

Figure 2 Comparative analysis of the number of hospitalizations related to lung cancer, the number of lung biopsies, and the number of bronchoscopies performed between March and December over the years 2017-2021

There were no significant statistical differences in age, sex and tumor staging between the three groups. However as shown in Table 1 patients in Group2 had a significant longer pre-hospital delay with a mean of 7, 02±2,06 months and higher performance status score 3-4 (64,6%) compared to the other Groups 1,3 (p < 0.000). Moreover the number of

cancer hospitalization, bronchoscopies per year including bronchoscopies and other biopsies with pathological confirmation dropped significantly in 2020 ($p < 0.000$).**Figure 2**

Histologically, 306 (86.9%) patients had NSCLC, while 46 (13.1%) had SCLC. Although there have been no differences in the cancer subtypes, a slight statistically significant increase in the number of SCLC has been noticed in 2020 ($p < 0.000$).

4. Discussion

With a growing number of COVID-19 patients requiring hospitalization, collateral effects such as restricted healthcare access and service provision must also be taken into consideration. Consequently, hospital activities required to diagnose and treat diseases, including cancer, has been hindered. In previous pandemics the H1N1 Influenza A virus epidemic in 2009 had an impact on cancer treatment with a decrease in the number of cancer surgeries performed [6]. Furthermore higher mortality was reported among patients with cancer, compared with that observed in the general population [7]. During the COVID-19 pandemic international reports showed a significant increase in the number of deaths from non-COVID-19 causes compared with the same period in the past [2].

According to Dinmohamed and al. the number of newly registered cancer patients in the Dutch National Cancer Registry decreased by about 25% in the period from March to May 2020 compared with the year before [3]. Lung cancer remains one of the most common and mortal malignancies. However, the effect of the COVID-19 pandemic on lung cancer management is not clear. Despite raising concern in the global medical and scientific community on the subject, there is still a major lack of studies in the African continent exploring the diagnosis and treatment of lung cancer during the COVID-19 pandemic. To our knowledge, this is the first Moroccan study to assess the impact of the COVID-19 pandemic on lung cancer diagnosis.

In our study, beside a reduction of 36% in newly diagnosed lung cancer patients, we also noticed that number of hospitalization, bronchoscopies and other biopsies performed dropped significantly in 2020 compared with the previous years ($p < 0.000$).Additionally, patients in Group2 had a significant longer pre-hospital delay with a mean of 7, 02±2, 06 months. Similarly, findings from the United Kingdom show a serious decline in the referral of cancer suspected cases during the COVID-19 pandemic [8, 9]. In another Chinese survey the proportions of lung cancer patients who were diagnosed based on symptoms and physical examination in the epidemic group were 34.2 and 18.2%, respectively vs 41.7 and 58.3%, respectively in the pre-epidemic group ; indicating that COVID-19 pandemic had a significant impact on the screening of lung cancer [10]. Furthermore a multicenter Italian study conducted by L. Cantini and al pointed out a reduction (6.9%) of newly diagnosed LC cases in 2020 compared with 2019 (1523 versus 1637, P ¼ 0.09) [11]. A Canadian retrospective chart review study comparing lung cancer trajectory before and during the COVID-19 pandemic, found that referral to a lung cancer specialist and subsequent diagnosis of lung cancer declined by 34.7% during the pandemic[12].In terms of the diagnostic methods used, a Spanish retrospective and observational study detected a slight decrease in the diagnoses reached with the aid of endoscopic and surgical techniques, as well in staging by invasive methods (23.9% in 2020 vs. 29.2% in 2019 and 27.1% in 2018) concluding to less use of endoscopic techniques in the course of the Covid-19 pandemic [13].

After the launch of first-level response to public health emergencies, hospitals in Morocco and across the world entered a state of emergency and strict prevention. Control measures were then deployed to prevent nosocomial infections which consequently contributed to the decrease in the number of hospitalizations, bronchoscopies and biopsies performed to diagnose lung cancer. Moreover, the psychological panic due to the spread of COVID-19 among the population made the patients worried about cross-infections and contamination in hospitals increasing the difficulty and complexity to access health care systems globally. A survey on patients with lung cancer who participated in a clinical trial in Taiwan during the SARS outbreak reported that about 64% of the patients were reluctant to visit a hospital out of fear for infection, and about 4% of the patients decided to discontinue all treatment due to concerns of infection [14]. All these results show that the persistence of the pandemic has a drastic impact on the diagnosis and treatment of patients with lung cancer.

Smoking remains the first risk factor for lung cancer; in our study we also noted an increase in second-hand smoke exposure during the pandemic and the year after ($p < 0.000$). In fact smoking behaviors changed during the COVID-19 lockdown as it has been described in many studies [15, 16].This can be interpreted as a result of the social distancing policies caused by the pandemic, forcing people to spend more time in their homes with more exposure to passive smoking [17].

In a multicenter cohort conducted by Park JY and al, the proportion of patients with stage III–IV non-small-cell lung cancer (NSCLC) significantly increased (2020: 74.7% vs. 2017: 57.9%, 2018: 66.7%, 2019: 62.7%, p = 0.011) assuming that the percentage of patients with more advanced stage cancers among newly diagnosed NSCLC patients during the pandemic was higher than that of previous years [18]. In our study, although (NSCLC) remains the most dominant lung cancer subtype, a slight statistically significant increase in the number of SCLC has been noticed in 2020 ($p < 0.000$). However no differences concerning tumor staging has been described between the 3 groups with most patients being classified as stage IVA-IVB through all the years (2017-2019: 73,9% vs. 2020: 85,4% vs 2021: 80,8%, p=0,151). According to the Eastern Cooperative Oncology Group, lung cancer patients during the covid-19 pandemic had higher performance status score 3-4 (64,6%) compared with the other Groups 1 and 3 ($p < 0.000$).

All these results conclude that despite the fact lung cancer being public health issue in Morocco, a lot of patients fail to consult early and face many psychological, socioeconomic, and familial obstacles to receive the required diagnosis and treatment which probably explains the advanced staging of the disease [19]. It is clear that theCovid-19 outbreak made this situation even worse. Moreover the lack of a national lung cancer screening program with prevention and early detection strategies makes it hard to access lung cancer control in developing countries [20]. Although several worldwide reports pointed out the negative outcome of the COVID-19 pandemic on treatment process by postponing or canceling anticancer therapies or surgeries [21], data on the impact of the pandemic on the various cancer therapeutic modalities within the African region remain sparse. More work needs to be done to explore how lung cancer treatment has been affected in some settings across the continent especially in Morocco [22].We acknowledge our work has potential limitations as a retrospective study; our analysis didn't include all the private medical facilities in the city of Marrakech that continued to receive some lung cancer patients through the lockdown. We also recognize that a long-term follow-up is required to evaluate the prognosis of patients with a delayed diagnosis of lung cancer.

5. Conclusion

From our results we conclude that the COVID-19 pandemic was responsible of a significant delay in the diagnosis of lung cancer in the region of Marrakech with a decrease in newly diagnosed LC cases. We also observed that less endoscopic techniques such as bronchoscopies and biopsies were performed in the course of pandemic and although no significant difference has been noted regarding tumor staging, lung cancer patients seemed to have higher performance status score 3-4 during 2020. There is no doubt the COVID-19 outbreak was a huge wakeup call to all the nations worldwide and while its repercussions on cancer care will likely be felt for decades to come, establishment of experts' consensus and application of national recommendations is mostly required to face the outcomes. These results also emphasize the urgent need to create a safe healthcare system providing effective clinical services to patients with serious diseases such as cancer during possible epidemics.

Compliance with ethical standards

Acknowledgments

Pr. AMRO, Dr. SAIDI participated in design and development of the study; analysis and interpretation of data; writing of the article, or critical analysis leading to significant changes in intellectual content; final approval of the submitted version after critical review. Dr Chaynez RACHID, Dr Houssam BIBORCHI, Pr Oussama FIKRI, Dr Adil MANSOURI and Pr Mohamed AMINE participated in the analysis and interpretation of data

Disclosure of conflict of interest

All the authors: Imane SAIDI, Chaynez RACHID, Houssam BIBORCHI, Oussama FIKRI, Adil MANSOURI, Mohamed AMINE, Lamyae AMRO report no conflict of interest in relation to the subject matter.

Statement of ethical approval

The present research work does not contain any studies performed on animals/humans subjects by any of the authors.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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