Original article

Diagnostic delay in lung cancer in Morocco: A 4-year retrospective study

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ABSTRACT

Background: Lung cancer is a major cause of morbidity and mortality worldwide. The diagnosis of lung cancer is complex and can be easily missed or delayed. The aim of this study is to describe the delay in diagnosis and evaluate the factors associated with diagnosis delay.

Methods: All patients diagnosed with primary lung cancer at Moulay Youssef University hospital in Rabat from January 2014 to December 2017 were investigated retrospectively. Data relating to patient characteristics, tumor characteristics, and all dates of visits and investigations were collected. Multivariate linear regression analysis was used to identify risk factors linked to delayed diagnosis.

Results: A total of 81 patients were included (81,5% were men). Around 85.2% of patients presented lung-related symptoms. Cough and dyspnea were the most common symptoms. The median time of the patient presentation was 75 days (interquartile interval (IQI) = 30–150 days), patient referral time was 08 days (IQI = 02–14 days), diagnosis time was 21 days (IQI = 14–22 days). In multivariate analysis, a higher age (p = 0.044) and weight loss (p = 0.038) were associated with an increased presentation patient time. Asthma (p = 0.004) and chronic obstructive pulmonary disease (COPD) (p = 0.040) were significantly associated with delayed referral time. Diagnosis time was longer in patients with non-suspected Chest-X ray (p = 0.045) and earlier in patients diagnosed with computed tomography-guided biopsy (p = 0.030).

Conclusion: Intervals of diagnosis were significantly delayed and highly affected by patients and diagnostic times. Thus, the results emphasize the extreme need to develop efficient strategies to improve lung cancer diagnosis intervals.

1. Introduction

Lung cancer is a serious problem of public health worldwide.[1] Over the past century, lung carcinoma has grown from a rare disease to the leading cancer and the most common cause of cancer death in the world,[2] registering 2.2 million new cases and 1.8 million death by 2020.[3] In Morocco, lung cancer is the deadliest cancer for both sexes.[4] This disease will continue to rank first in the list of cancers in Morocco, in 2040, with a rate of mortality of 16/100 000.[4]

Lung cancer is often diagnosed in symptomatic patients.[5] The core symptoms of lung cancer include cough, dyspnea, chest pain, fatigue, hemoptysis, and weight loss.[6] Those symptoms are very common in general practice, it would be difficult to distinguish them from the

symptoms of other respiratory diseases.[6] Such overlap of symptoms could cause delays in diagnosis of lung cancer,[7] which may alter the tumor stage and, in that way, patients lose their chance for surgery. In addition, cancer patients face many psychological, socioeconomic, and familial obstacles to receive the required diagnosis and treatment.[8]

Shortening the delay times might increase the number of early-stage cancer, and consequently, improve survival. In the literature, several studies have focused on the study of diagnosis delays of patients with lung cancer.[5–8] Some countries have implemented guidelines for the optimal timing of diagnosis and treatment of lung cancer.[9] The British Thoracic Society (BTS) has made various recommendations concerning the diagnosis and treatment delays for patients with lung cancer.[10] The American College of Chest Physicians evidence-based clinical practice

guidelines suggest that efforts should be made to deliver timely care,[11] without presenting specific guidelines on the timeliness of lung cancer.[12] American guidelines recommend timeframes of 10 days for specialist review.[9] Standards from Australia recommend 14 days maximum delay between first general practitioner (GP) referral and first lung cancer specialist appointment, and between diagnosis to treatment.[13] A systematic review including 49 studies concluded that times to diagnosis and treatment of lung cancer often exceeded recommendations.[14]

In Morocco, little is known about delays in the diagnosis of primary lung cancer. This study aimed to explore the presentation of symptoms in Moroccan patients with primary lung cancer. Description of times from the onset of symptoms to diagnosis was also performed. An assessment of causes related to delayed diagnosis was also explored.

2. Material and methods

This study was conducted at Moulay Youssef hospital affiliated with the Ibn Sina University Hospital center in Rabat. It is the largest hospital specializing in respiratory disease in Morocco.

Access to this hospital is only possible by referral from primary care or directly through the emergency department.

After lung cancer diagnosis, patients are transferred according to the stage of the disease to the thoracic surgery department of the Ibn Sina hospital if the disease is operable, otherwise to the national oncology institute.

We adopted a retrospective study of all patients with primary lung cancer diagnosed between January 2014 and December 2017. Patients with other pathology, those with metastatic lung cancer from other organs, and those with non-found or incomplete records were excluded from the study.

The following data were extracted from the patients' file: sex, age, social security status, address, smoking habits, symptoms, comorbidities, pathology method, tumor histology, tumor stage, date of first symptoms, date of first general practitioner (GP) visit, date of first pulmonary-disease specialist visit, date of diagnosis.

We adapted operational definitions to extract data about time intervals from first clinical presentation until diagnosis for lung cancer.[15,16] Fig. 1 describes these time intervals.

Patient presentation time was defined as the time from the onset of symptoms until the first visit to a general practitioner (GP). If patient presentation interval exceeded 30 days, it was considered indicative of a patient's delay.[17,18]

Referral time was defined as the time between the first GP visit and the first specialist visit. Diagnosis time was defined as the time between the first specialist visit and the date of diagnosis.
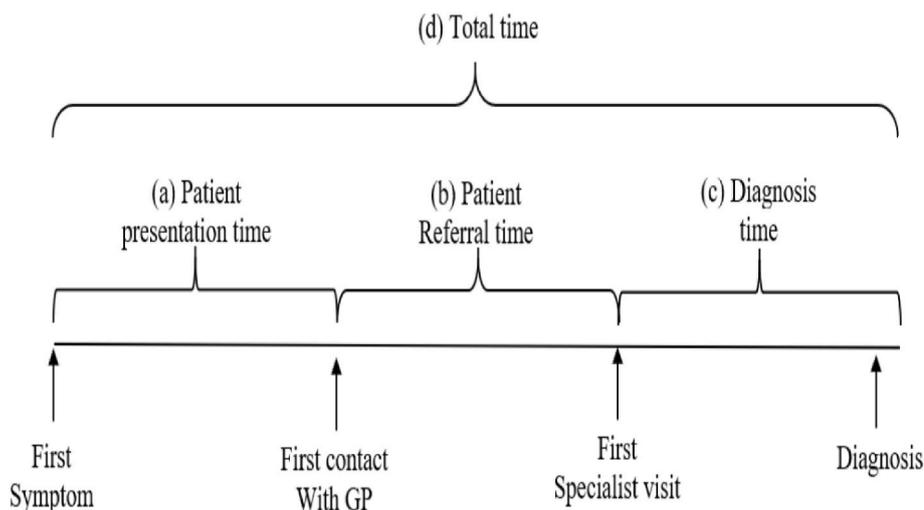
Based on the British Thoracic Society (BTS) recommendations, a referral time longer than two weeks and diagnosis time that exceeding two weeks are considered to be late.[8] Considering these recommendations, a time between the first visit to a general practitioner (GP) and the date of diagnosis over four weeks was taken as a criterion for doctor delay. A time from the onset of the first symptom and the date of diagnosis that exceeds 58 days (4 weeks +30 days) was considered as a criterion for the total delay.

Continuous variables were presented as median and interquartile interval. Categorical variables were presented as frequencies and percentages. The normality of all quantitative variables was verified. The main possible factors of delay were analyzed by uni- and multivariate linear regression analysis using a selection of factors associated ($p \leq 0.30$) with delay in univariate analysis. However, the factors sex, smoking, and distance to the nearest cancer center were forced into the model. A p-value of less than 0.05 was considered significant. All data were analyzed using Jamovi version 2.0.0.

3. Results

From 286 patients hospitalized during the study period, 102 patients were diagnosed with primary lung cancer and 184 with other thoracic malignancy or non-malignant conditions. Among patients diagnosed with primary lung cancer, 21 patients were excluded because of missing data. In total, 81 patients with primary lung cancer were included in this study, consisting of 66 (81.50%) men and 15 (18.50%) women. The mean age at diagnosis was 58.34 ± 10.01 years (range, 33–85 years). Characteristics of the study population are listed in Table 1. Patients came mainly (81.50%) from primary care, and were referred to the hospital because of a suspect X-ray in 65.15% of cases, hemoptysis, chest pain, and cough in 13.63%, 10.60%, and 9.10% of cases, respectively.

More than two-thirds (76.54%) of the participants were smokers. The mean pack-years of smoking was 38.2 ± 18.42 pack-years. The patients were presented at the hospital with many different symptoms. The majority (85.18%) of them reported respiratory symptoms before the diagnosis. Cough was the most common symptom, followed by dyspnea, chest pain, and hemoptysis, with 74.1%, 61.73%, 51.85%, and 50.61%, respectively. Eight of these patients had also symptoms related to brain metastases. Only 13.58% of patients had atypical symptoms such as lack of appetite, fever, or fatigue. One patient was asymptomatic and was diagnosed by chance. A pulmonary lesion was found on a routine chest X-ray. Table 2 shows the presentation of symptoms of the study population.

The median patient presentation time was 75 days (IQI = 30–150 days). This time was ranged from 7 days to a maximum of 365 days.

Fig. 1. Components of the times from the first symptoms to diagnosis

Patient presentation time (a) is the time from the onset of symptoms until the first visit to a general practitioner. Referral time (b) is the time between the first GP visit and the first specialist visit. Diagnosis time (c) is the time between the first specialist visit and the date of diagnosis. Total time (d) is the time from the onset of the first symptom and the date of diagnosis.

Table 1

Main characteristics of patients in Moulay Youssef hospital in Rabat.

Characteristic	N	%
Sex		
Male	66	81.48
Female	15	18.52
Age, years		
Adult (≤60 year)	53	65.43
Elderly (>60 years)	28	34.57
Health insurance		
Yes	76	93.83
No	5	6.17
Traveling distance to nearest cancer center (Km[a])		
≤ 30	54	66.67
>30	27	33.33
Smoking habits		
Smokers	62	76.54
Nonsmokers	19	23.46
Respiratory symptoms at presentation		
Yes	69	85.18
No	12	14.82
Other pulmonary diseases		
COPD[b]	28	34.57
Tuberculosis	24	29.60
Asthma	10	12.34
Pneumonia	08	9.88
Diagnostic method		
Bronchoscopy	56	69.14
CT-guided biopsy[c]	12	14.81
Pleural biopsy	10	12.35
Lymph node biopsy	03	3.70
Tumor histology		
Adenocarcinoma	51	62.96
Squamous cell	14	17.29
Small cell cancer	09	11.11
Others	07	8.64
Disease stage		
II	7	8.6
IIIA	13	16.0
IIIB	12	14.8
IV	49	60.50

[a] Km: Kilometer.
[b] COPD: Chronic Obstructive Pulmonary Disease.
[c] CT-guided biopsy: Computed Tomography guided biopsy.

Table 2

Presentation of symptoms of patients in Moulay Youssef hospital in Rabat.

Symptom	No. Cases	%
Cough	60	74.10
Dyspnea	50	61.73
Weight loss	42	51.85
chest pain	41	50.61
Lack of appetite	25	30.86
Fever	21	25.92
Hemoptysis	21	25.92
Condensation syndrome	17	20.98
Fatigue	11	13.58
Cerebral symptoms	8	9.87
Musculoskeletal pain	6	7.41
Visible lymph node on the neck	5	6.17
Dysphonia	4	4.94
Anorexia	3	3.70
Vena cava superior syndrome	3	3.70
No symptoms (incidental finding)	1	1.23

Only 14.81% of patients visited the doctors within one month from the onset of symptoms. On univariate analysis, there were no significant differences in time taken to consult between symptomatic and asymptomatic patients or between smokers and never smokers. Also, sex, age, cough, hemoptysis, and history of previous no malignancies lung disease were not significantly associated with earlier consulting in GPs. After adjusting with other variables (Table 3), there is a significant difference in patient presentation time between patients aged 60 years or less and

Table 3

Univariate/multivariate linear regression analyses of factors associated with patient presentation, patient referral, and diagnosis times.

Variables	Univariate analysis β (95% CI)	P-value	Multivariate analysis β (95% CI)	P-value
Patient presentation time (n = 66)				
Sex[a]				
Men-women	−10.1 (−76.4 to 56.2)	0.762		
Age (years)				
≤ 60 - > 60	−33 (−83.6 to 17.5)	0.197	−56.8 (−112.02 to −1.57)	0.044
Smoking[a]				
Yes- no	4.98 (−56.1 to 66.0)	0.871	−22.92 (−122.56 to 76.71)	0.637
Adenocarcinoma				
Yes- no	−29.2 (−83.6 to 25.3)	0.289		
Chest pain				
Yes- no	32.4 (−18.2 to 82.9)	0.206		
Weight loss				
Yes- no	42.7 (−7.93 to 93.4)	0.097	53.8 (3.00–104.52)	0.038
Patient referral time (n = 66)				
Respiratory disease				
Yes- no	8.38 (−4.03 to 20.8)	0.182		
Tuberculosis				
Yes- no	9.33 (−5.00 to 23.7)	0.198		
COPD				
Yes- no	9.60 (−3.24 to 22.4)	0.140	18.74 (0.280–37.19)	0.040
Asthma				
Yes- no	24.0 (5.87–42.1)	0.010	28.67 (9.441–47.90)	0.004
Distance[a]				
≤ 30 km- > 30 km	1.64 (−11.56 to 14.8)	0.805	−4.47 (−18.144 to 9.21)	0.516
Diagnosis time (n = 81)				
Sex				
Men-women	3.87 (−3.72 to 11.4)	0.313	2.21 (−5.839 to 10.251)	
Age				
≤60 years- > 60 years	−3.64 (−9.53 to 2.24)	0.222	−3.90 (−10.716 to 2.918)	
Non-suspected chest X-ray				
Yes- no	7.48 (0.765–14.2)	0.030	7.01 (0.158–13.855)	0.045
COPD				
Yes- no	5.91 (−0.181 to 12.0)	0.057	4.64 (−2.018 to 11.293)	
CT-guided biopsy				
Yes- no	7.48 (0.765–14.2)	0.030	−9.97 (−18.93 to −1.000)	0.030
Distance[a]				
≤ 30 km- > 30 km	4.54 (−1.67 to 10.7)	0.150	5.58 (−1.231 to 12.38)	0.107

[a] Forced factors into the model.

those aged more than 60 years (p = 0.044). Also, a significant difference was noted in patients presenting a weight loss (p = 0.038).

From the first contact with the general practitioner (GP) until the first visit to the specialist, the median time was 08 days (IQI = 02–14 days). Over two-thirds (74.24%) of participants were referred within two weeks. GPs wrote a referral on the same day of the visit for twenty-nine patients. On univariate analysis, neither distance to the nearest cancer center, asthma nor COPD was associated with patient referral time. After adjusting with other factors (Table 3), both asthma (p = 0.004) and COPD (p = 0.040) were significantly associated with longer referral time.

The median time between the first visit to a specialist and diagnosis

was 21 days (IQI = 14–22 days). Only 27.16% of cases had the diagnosis within two weeks. When exploring factors of diagnostic delay (Table 3), were increased in patients with non-suspected chest-X ray (p = 0.04) and earlier in patients diagnosed with CT-guided biopsy (p = 0.003).

The median doctor time was 33.5 days (IQI = 20–43 days). Over half of cases (54.55%) had a delayed doctor time. The median total time from the first symptom to the final diagnosis (the sum of all times) was 123 days (IQI = 63–202 days). Over three quarters (81.82%) of patients had a delayed total time. The total time was not affected by any of the studied factors.

4. Discussion

To our knowledge, this study is the first in Morocco to calculate delays using a validated model about time intervals from the onset of the first symptom until diagnosis and assess factors of these delays.

Almost the majority of our patients were symptomatic at the first presentation, cough was the most common symptom. Several studies found that cough is frequent in patients with lung cancer.[7,19] Also, cough in patients with lung cancer is more severe than patients with chronic obstructive pulmonary disease (COPD) and asthma.[20]

Based on our results as well as the results of other studies around the world, the patient interval in our series was very delayed. The majority of published studies find a shorter time except for a cross-sectional study in the UK that found a median of 99 days.[21] In Turkey and Tunisia, the mean patient delay was, respectively, 49.9 days and 82.9 days.[18,19] In Sweden, Finland, Malaysia, Denmark, and Netherlands, the median was respectively 11 days, 14 days, 60 days, 33 days, and 22 days.[7,17,22–24]

We found no significant differences in the time taken to consult between patients with respiratory symptoms and those without respiratory symptoms. Various reasons may be suggested to explain this. The main is that patients did not interpret these symptoms, and therefore did not react in a timely way. A cross-sectional study found that patients were unaware of the symptoms related to lung cancer and did not consider them as an indication of this disease.[21]

In our study, factors associated with time to consult was weight loss and elderly age. A French team found no difference regarding the patient presentation time between elderly and younger patients with lung cancer.[25]

On the other hand, the referral time in our study appears acceptable. 74.24% of patients were referred within the standards of international recommendations. For only 10.6% of patients, the time was longer than one week. A Dutch study found a median of 7 days, and a Turkish study an average of 61.6 days.[18,24] Our results showed that previous lung diseases, in particular asthma and COPD, were associated with a delayed referral time. Many studies showed that comorbidities are major contributors to delay.[7,9,18]

Regarding the diagnosis delay, only 27.16% of the cases were consistent with the British Thoracic Society (BTS) recommendations.[10] Our median of 21- day was longer than 9 days, and 10 days reported respectively from Sweden and France.[17,26] Studies performed in Turkey and the USA found an average time between the visit to a pulmonary disease specialist and diagnosis of 20.4 days and 43 days, respectively.[18,27] Non-suspicious chest X-ray was associated with delayed diagnosis time in our series. This association has been found previously in other studies.[7,28] Conversely, when comparing the method of diagnosis, diagnosis time was earlier in patients diagnosed with CT-guided biopsy, which may result in waiting times required at the hospital for each diagnostic method.

Distance to the cancer center was not associated with longer delays in our study. A review of the literature found that distance is an important factor influencing access to timely and appropriate diagnosis of cancer.[8]

It appears from our results, that patients take a long time to consult a doctor, undergo investigations, and then have a diagnosis. The majority of our patients were in a late stage of the disease. Results from a previous study showed that patients diagnosed in earlier stages had better clinical outcomes.[29] Also, delays might be stressful for both patients and families.[30] Some studies seem very promising to shortness delays. The time to treat Program of Canada has reduced the delay from 128 to 20 days for the entire management process and consequently has generated growing satisfaction in patients and professionals.[31] In the USA, an experience using nurse navigation improve the time between the suspicion of cancer until treatment from 136 days to 55 days.[32] A recent study has shown that Rapid lung cancer diagnosis units have reduced delays and positively impacted the quality of care.[33]

The major strengths of our study are its originality and the reliable collection of data from several sources: patient charts, reports from general practitioners and specialists, and reference files. In addition, we have used valid models for the presentation of the different intervals. Nevertheless, the retrospective nature of the study constitutes an important limitation, as it did not provide information such as the educational and socioeconomic level, that has a significant impact on the delays of lung cancer diagnosis.

5. Conclusion

This study showed an important aspect of lung cancer healthcare. Intervals of diagnosis were significantly delayed and highly affected by patients and diagnosis times. Thus, the results emphasize the extreme need to develop efficient strategies to improve lung cancer diagnosis intervals, based on general public awareness, particularly in high-risk groups, of the importance of certain key symptoms related to lung cancer, and the shortening waiting times for investigations.

Author contributions

Ouassima Erefai: Conceptualization, methodology, investigation, data curation, formal analysis, writing-original draft preparation, writing-review an editing. Abdelmajid Soulaymani: Conceptualization, investigation, writing-review and editing. Abdelrhani Mokhtari: Conceptualization, investigation, writing-review and editing. Majdouline Obtel: Conceptualization, investigation, formal analysis, writing-review an editing. Hinde Hami: Conceptualization, methodology, investigation, formal analysis, writing-original draft preparation, writing-review an editing.

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Declaration of competing interest

The authors have no conflicts of interest to declare for this study.

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