Original Paper

Retrospective Study of Lung Tumor Cases Presenting at a Large Tertiary Hospital in Romania between 2017 and 2020

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ABSTRACT: Lung cancer is a major health concern worldwide. A rise in smoking incidence amongst both genders, increased exposure to air pollutants and unhealthy lifestyle choices steadily contribute to this global situation. Our aim was to assess the main characteristics of this type of cancer through a retrospective analysis at a major referral center. We selected valid and complete electronic medical records of patients admitted between 2017 and 2020 at the Emergency County Hospital of Craiova, one of the largest hospitals in Romania and a major referral center for the region of Oltenia. We obtained ethical approval from both the hospital and the University and analyzed anonymized records by ICD-10 diagnostic code, extracting gender and age data, as well as associated conditions, length of stay, as well as the medical departments where the patient was hospitalized. Our results showed an increased incidence amongst men, with the majority of cases between 50 and 70 years of age. Median hospitalization period was of 6 days, with higher values for oncology and the lowest in thoracic surgery. Distant metastases, pleurisy and hemoptysis were the most prevalent comorbidities encountered. In conclusion, our study presents important data on the main characteristics of lung cancer patients in Romania.

KEYWORDS: *Lung cancer, incidence, retrospective analysis, hospitalization time, comorbidities.*

Introduction

Lung cancer cases and deaths caused by it are increasing globally.

In 2020, GLOBOCAN estimated 2.2 million new cases (11.6% of all cancers) and 1.79 million deaths (18% of total cancer deaths), higher than those reported in 2012 (1.8 million new cases and 1.6 million deaths) becoming the most common cause of cancer deaths in men and women combined [1].

For females, it is the fourth most common type of cancer and the second most common cause of cancer death.

The prognosis remains reserved, with 15% survival at 5 years [1-3].

Regarding the incidence of lung cancer in EU countries, depending on the age standardized rate (worldwide) for both genders, there are important differences regarding the risk of developing this disease in different countries.

For example, approximately three out of 100 men in Sweden, Cyprus, Finland and Malta will develop lung cancer during their lifetime, while this number rises to nine out of 100 in Hungary and seven per 100 men in Poland, Belgium, Croatia, Romania, Lithuania and Latvia [4].

The incidence rate in 23 European countries is higher than the world average (23.1 per 100,000).

Hungary has the highest incidence of lung cancer, with a standardized age rate of 51.6 per 100 [5].

In the EU, Hungary is followed by Denmark, Poland, the Netherlands and Belgium.

These countries also have high incidence rates.

Lung cancer is the highest incidence of cancer in four European countries (Greece, Hungary, Poland and Romania) and the second largest in Bulgaria, Croatia, Latvia and Lithuania [3-6].

Aim

Our aim was to assess lung tumor incidence in an important multidisciplinary referral center and to identify the main risk factors, comorbidities, most important concurrent symptoms, as well as to assess the usual follow-up route of these patients, once tumors were identified.

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Patients and Methods

Study design and methodology of inclusion

We retrospectively included all patients that were hospitalized with lung tumors, between January 1st 2017 and September 30th 2020 at the Emergency County Hospital of Craiova (ECHC), Romania.

We performed a search in the patient management software of the hospital for ICD-10 diagnostic codes pertinent to malignant lung tumors, as follows: C34.1 (Malignant neoplasm of upper lobe, bronchus or lung), C34.2 (Malignant neoplasm of middle lobe, bronchus or lung), C34.3 (Malignant neoplasm of lower lobe, bronchus or lung), C34.8 (Malignant neoplasm of overlapping sites of bronchus and lung), C34.9 (Malignant neoplasm of unspecified part of bronchus or lung).

Additionally, we performed a search for the R04.2 diagnostic code-hemoptysis, in order to assess the number of malignancy-related cases in regards to total number of presentations for this diagnosis.

The anonymized records were retrieved and processed on-site, on a dedicated computer, as per the standard protocol for retrospective studies.

No patient personal data was retrieved or processed off-site, thus no further patient consent was required.

Our study was approved by the Ethical Committee of the University of Medicine and Pharmacy of Craiova (approval 42 from June 17th 2020) and that of the ECHC (approval 26659 from July 8th 2020).

Once initial records were retrieved, we also looked for second admissions under one of the five diagnostic codes in order to follow-up on individual cases.

These data were included in our subgroup analysis. We then proceeded to check secondary free-form diagnoses recorded in the computerized system at discharge.

We also recorded demographic data (age and gender), as well as the medical department where patients were admitted, as well as admission and discharge dates.

Statistical analysis

All statistical calculations were performed in GraphPad Prism (GraphPad Software, USA).

We presented data as either median, minimum and maximum values, with upper and lower percentiles, or as mean, standard deviation and standard error of means.

We used the unpaired t test to assess differences between means, the nonparametric Mann Whitney test to compare the distributions of two unmatched groups and the ANOVA test to assess differences between multiple means.

Statistical significance was achieved at p values below 0.05.

Results

We discarded 12 records as incomplete, and initially found 1571 records with one of the diagnostic ICD-10 codes within the timeframe.

After eliminating repeated entries for the same patient, we found 970 individual cases with at least one presentation.

Of these, 764 (78.8%) were men and 206 women (21.2%).

Further, 215 patients (18.14%, 167 men and 48 women) presented two or more times with diagnostic codes specific for malignant lung tumors.

The majority of these had two visits (102 patients, 71 male); 72 had three (60 male), 24 had four (18 men) and 17 patients (10 men) presented five or more times for various procedures, under the same diagnostic code.

A diagram of the study can be found in Figure 1.

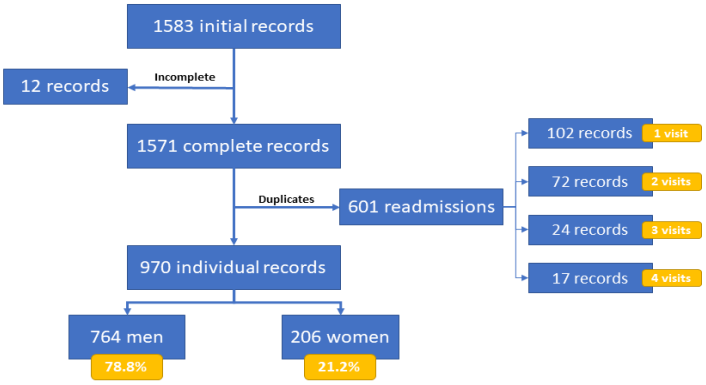

Figure 1. Diagram of the study protocol.

The distribution of patients according to diagnostic codes is presented in Table 1.

The overall gender distribution was similar in each subgroups, with the exception of C34.2 (Malignant neoplasm of middle lobe, bronchus or lung), where we only had 41 cases (4.22% of the whole lot).

Table 1. Distribution according to each type of diagnostic code. N=number, %=percentage from total, according to diagnosis. % from total=percentage of each code, from total number of cases.

	Men		Women		Total	
	N	**%**	**N**	**%**	**N**	**% from total**
C34.1	173	*75.22*	57	*24.78*	**230**	*23.72*
C34.2	30	*73.17*	11	*26.83*	**41**	*4.22*
C34.3	119	*79.33*	31	*20.67*	**150**	*15.46*
C34.8	241	*79.80*	61	*20.20*	**302**	*31.14*
C34.9	201	*81.38*	46	*18.62*	**247**	*25.46*
All lung tumors	**764**	***78.76***	**206**	***21.24***	**970**	***100%***

We found that the gender ratio was constant in all subgroups, irrespective of the number of visits, and distributed similarly to the entire lot (chi square test, p=0.44).

Results of the statistical analysis are presented in Figure 2 and Table 2.

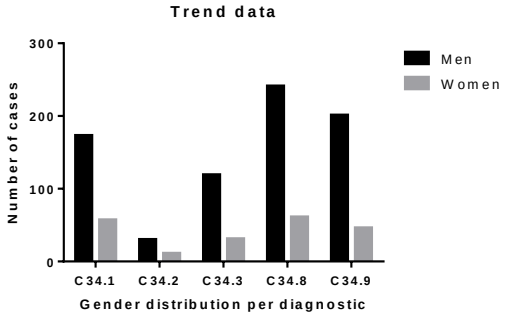

Figure 2. Distribution according to each type of diagnostic code. The trend showed no significant difference between the five diagnostic codes used in our retrospective analysis.

Table 2. The chi-square test showed no statistical difference between the gender distribution in each lot; therefore, we could conclude that cases followed the same distribution trend, irrespective of diagnostic.

Chi-square	
Chi-square, df	3.728,4
P value	0.44
P value summary	ns
Statistically significant? (alpha<0.05)	No

We then proceeded to analyze age distribution within our lot.

Median age was 66 for men and 68 for women, with minimum ages of 23 and 36 years, and maximum of 91 and 92 years, respectively (Table 3).

The histogram of age distribution per gender is presented in Figure 3.

We found similar median ages for both men and women (Unpaired t test, p=0.33) in our lot (Table 4 and Figure 4).

Table 3. Descriptive statistics of the median ages within our lot, according to gender.

	Men	**Women**	**Entire lot**
Number of values	**764**	**206**	***970***
Minimum	23	36	*23.0*
25% Percentile	61	60	*60.0*
Median	66	68	*66.0*
75% Percentile	72	74	*73.0*
Maximum	91	92	*92.0*

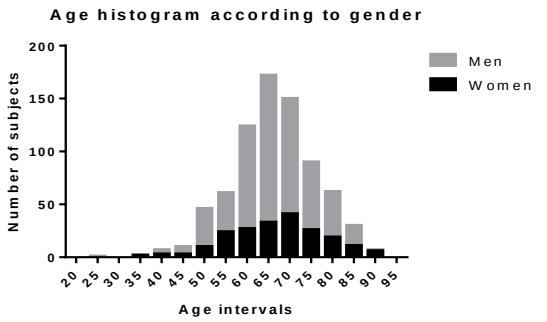

Figure 3. Histogram of age distribution according to each gender. We can observe that the same trend is kept irrespective of age.

Table 4. Statistical data-Unpaired t test showed no difference in age distribution, according to gender.

Unpaired t test	
P value	0.33
P value summary	*ns*
Significantly different? (P<0.05)	No
One- or two-tailed P value?	Two-tailed
t, df	t=0.96 df=964

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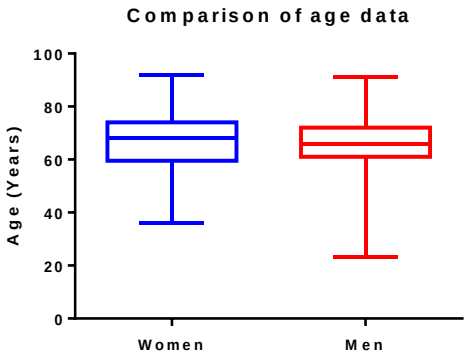

Figure 4. Age comparison according to gender. No significant differences were seen between men and women in our study lot.

We found 401 cases (41.34% of the entire lot) who had significant co-morbidities listed as secondary, free-form written diagnostics in the electronic records.

Their distribution can be found in Table 5.

We found that the trend in gender distribution remains close to that in the entire lot (chi square test, $p>0.05$).

The most common finding was the presence of metastases (248 cases, 25.56% of total and 61.84% of all complications).

Pleurisy was found in 12.59% of total cases (of which 2.79% associated with metastases) and accounted for 23.69% of all complications, while cases with hemoptysis with or without metastases accounted for only 3.09% of all cases.

However, we found 134 patients presenting for hemoptysis as primary diagnosis at ECHC within the same time-frame, separate from our study lot.

Thus, the 30 cases found in our study were equivalent to 22.39% of those who had a main diagnosis of hemoptysis.

Table 5. Distribution of each comorbidity/complication according to gender. Notations same as Table 1.

	Men		**Women**		**Total**	
	N	**%**	**N**	**%**	**N**	**% from total**
Metastases	194	*78.22*	54	*21.78*	**248**	*25.56*
Pleurisy	76	*80*	19	*20*	**95**	*9.80*
Hemoptysis	19	*70.37*	8	*29.63*	**27**	*2.79*
Metastases and pleurisy	22	*78.57*	6	*21.43*	**28**	*2.89*
Metastases and hemoptysis	3	*100*	0	*0*	**3**	*0.30*
All complications	**314**	***78.30***	**87**	***21.70***	**401**	***41.34***

We further analyzed cases according to the medical department where they were admitted. Data is presented in Table 6.

Overall, we could see that 53.92% of all patients presented for oncological treatment. From cases first presenting in pulmonology, 73 patients (50%) were re-admitted in thoracic surgery and 20 (13.69%) in oncology.

All cases from surgery were re-admitted to thoracic surgery.

Also, all cases with three or more presentations were admitted to oncology at some point.

Table 6. Distribution of cases according to medical department of admission. *-Oncology includes data from Radiotherapy; **-Pulmonology includes cases from the internal medicine department; ***-Surgery includes data from three separate clinics with ECHC.

	Men		**Women**		**Total**	
	N	**%**	**N**	**%**	**N**	**% of total**
Oncology*	425	*81.26*	98	*18.74*	**523**	*53.92*
Thoracic surgery	172	*81.51*	39	*18.48*	**211**	*21.75*
Pulmonology**	107	*73.29*	39	*26.71*	**146**	*15.05*
Surgery***	19	*70.37*	8	*29.63*	**27**	*2.78*
Other departments	41	*65.08*	22	*34.92*	**63**	*6.49*
TOTAL	***764***	***78.76***	***206***	***21.24***	**970**	***100***

The median length of hospitalization was 6 days (minimum 3 days, maximum 42 days).

We found significant differences in this regard between the medical departments where cases were first admitted (ANOVA test, $p<0.0001$).

Comprehensive date can be found in Tables 7 and 8.

A depiction of the distribution of hospitalization days according to medical department can be found in Figure 5.

Table 7. Descriptive statistics regarding the days of hospitalization per each medical department. Data is presented both as median with minimum and maximum values, as well as mean, standard deviation and standard error.

Department	Oncology	Thoracic Surgery	Pulmonology	Surgery	Other dept.	All dept.
Minimum	3	3	3	3	3	***3***
Maximum	42	26	30	15	32	***42***
Median	6	4	7	5	5	***6***
Mean	7.88	5.68	7.85	6.82	7.64	***7.35***
Std. Deviation	6.07	4.00	4.58	4.19	6.23	***5.50***
Std. Error	0.26	0.27	0.38	0.72	0.76	***0.18***

Table 8. The ANOVA test showed significant differences between median hospitalization periods depending on the medical department where patients were admitted.

ANOVA summary	
F	5.26
P value	<0.0001
R square	0.01334

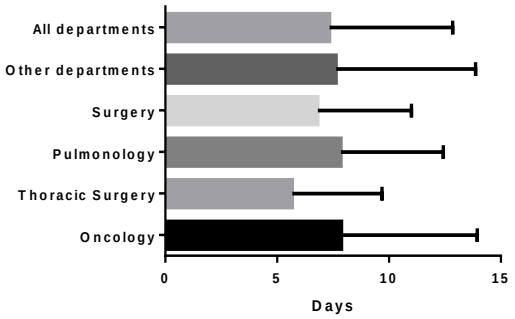

Figure 5. Graphical representation of the number of days per medical department. We could observe great variability in each group, unrelated to age or comorbidities.

Discussions

Primary malignant lung tumors continue to be a significant health burden worldwide.

With rising incidences due to increased exposure to environmental factors, lung cancer left undiagnosed for longer periods of time still associates with poor prognosis, increased hospitalization times and costs, as well as significantly decreased overall quality of life for patients, mostly irrespective of age.

In this study, we retrospectively investigated cases of primary bronchopulmonary malignant tumors that presented over a three year period at a major, regional, healthcare provider.

We followed the case repartition, number of comorbidities or associated conditions, number and length of presentations and extracted relevant data.

This is, to our knowledge, the first analysis of such cases performed at a medical center of this size, in our country.

We found lung cancer to be significantly more prevalent in men (gender ratio was 3.71:1 in favor of men) in our study group, with male subjects accounting for 78.8% of all cases.

This result was obtained irrespective of tumor location in respect to lung lobulation, age group or comorbidities.

A rise in incidence of lung cancer in women was observed in recent literature, and was associated with the increased prevalence of smoking among woman [7-9].

However, in all literature, figures were consistently higher for male patients, irrespective of tumor stage or mortality rate [7,8,10].

The particularity encountered in our study may be linked to cultural particularities, as smoking is more prevalent in our country in men of ages at which lung cancer is more prone to appear.

Our study population had similar median ages (66 years for men *versus* 68 years for women, overall median age 66 years old).

The majority of cases were encountered, for both sexes, between the 5^{th} and 7^{th} life decade.

This result is in line with literature; screening is usually recommended in intensive smokers (above 30 pack-year smoking history), aged 55 to 80 years [10].

A recent analysis of WHO data revealed that distant metastasis is the most reputable complication of lung cancer.

Pleural affect ranks second and hemoptysis third, in most literature.

We analyzed other diagnoses associated with lung cancer, focusing on the existing of metastases, Pleurisy, hemoptysis or a combination of two or more such conditions.

Since most patients were hospitalized for oncological treatment (overall 53.92% of the

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study lot). Both genders had the same statistical distribution for these conditions.

The percentage of each condition was in line with other research; metastatic tumors were the most common additional finding, since most cancers are unfortunately discovered at advanced stages [11].

Another aspect that we took into account in our study was length of stay within the hospital, correlating these data with the department and, subsequently, type of intervention required.

We found that oncological treatment required in median 6 days of hospital time, similar to pulmonology (seven days median time).

This can be easily explained by the series of investigations needed for other underlying conditions, as well as a more complex management.

In contrast, the lowest time to discharge was found in thoracic surgery (median of 4 days), which can be explained by fast recovery times following chest surgery, general absence of serious comorbidities in patients fit for procedures and, possibly, an overall low number of post-procedural adverse effects.

As our study did not account for histological subtype, we did not analyze hospitalization times in relation to either prognostic or therapeutic procedure within the guidelines; recent literature debates the use of immunotherapy in small-cell lung cancer, as well as the influence radiation dosage has over outcome and hospitalization time [12].

Finally we followed the cases that required multiple hospitalizations, finding 215 patients (22.16% of the study lot) that required more than one hospital visit.

The higher visit count was seen in oncological patients, being explained by the need for multiple chemotherapy sessions.

We found that 63.7% of the patients presenting first in pulmonology (93 of the 146 patients) were referred to either surgery or oncology, following suspicion or certain diagnosis of a lung tumor.

It was widely debated in recent literature how re-hospitalization and multiple-staged therapy influences costs and the prognostic of the disease [13,14].

One major limitation of our study was its retrospective nature.

It is well documented that electronic medical records can be incomplete or contain altered information due to transcription errors.

However, the electronic database kept within ECHC allows for rapid ICD-10 coding of the disease, as well as free-form written diagnoses by the attending physician.

Once exported, data was manually checked for integrity and consistency, and we eliminated all incomplete entries from our study.

Another limitation refers to the lack of pathology data for some of our cases.

All cases that had a presentation at the Department of Oncology and accounted for in our study had microscopic confirmation; cases that presented to Thoracic Surgery or Pulmonology generally underwent either surgery or bronchoscopy, in order to achieve diagnosis or to properly classify the tumor.

We did not, however, follow up on these results in our study as the planned analysis did not require it.

Finally, a minor limitation may have arisen from the fixed three-year timeframe allotted for the study.

This interval was chosen in order to guarantee the integrity of the data entered in the electronic system, since the pandemic conditions did not allow us to manually search paper records.

Conclusion

We conducted a three year retrospective study of patients presenting for lung tumors at a large tertiary referral center in Romania.

Our data showed the predominance of male patients aged 50 to 70 years, with a median hospitalization time of six days and an overall incidence of metastases, pleurisy and hemoptysis of 41.34%.

The majority of patients also presented with metastases, pleurisy or hemoptysis.

We found that 22.16% of the lot also required at least a second visit for either re-treatment or supplemental investigations.

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Conflicts of interest

The authors declare no conflicts of interests.

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