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Diagnosis of lung cancer by flexible fiberoptic bronchoscopy: a descriptive study

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Abstract

Flexible fiberoptic bronchoscopy (FFB) remains the most important minimally invasive method for the diagnosis of lung cancer (LC). We performed a retrospective study to assess the main endoscopic findings of malignant lung tumors in the large airways in a cohort of Romanian patients. The group consisted of 32 (84.21%) men and six (15.78%) women, with an average age of 64.63±6.07 years. The bronchoscopic examination allowed the detection and biopsy of 36 malignant lung tumors, and in two other cases, due to malignant atelectasis, the patients were sent to a Department of Thoracic Surgery, to perform the biopsy following the surgery. Histopathological (HP) examination revealed the presence of squamous cell carcinoma (SCC) in 19 (50%) patients, adenocarcinoma (ADC) in 11 (28.94%) patients and small cell lung cancer (SCLC) in eight (21.05%) patients. The macroscopic and microscopic analysis of the lung tumors showed that infiltrative forms were found in most cases (58.33%), followed by exophytic (mass) endobronchial lesions (22.22%) and mixed forms (19.44%). If most infiltrative forms were SCC (66.66%), the exophytic and mixed lesions were most frequently ADC (50% and 57.14%). The tumor lesions caused both malignant bronchial stenosis (57.89%) and malignant atelectasis (42.1%). The main mechanisms involved in bronchial malignant obstruction were endoluminal (50%), mixed (31.57%) and extraluminal (18.42%) mechanisms. In conclusion, FFB remains the main method of diagnosing LC in the large airways. The most common macroscopic appearance of lung tumors revealed by bronchoscopy was the infiltrative appearance. In half of our patients, the malignant bronchial obstruction was achieved by endoluminal mechanism. The most common pathological form found in our patients was the SCC, as described in half of the investigated patients.

Keywords: bronchoscopy, lung squamous cell carcinoma, lung adenocarcinoma, small cell lung carcinoma.

Introduction

Although the incidence of lung cancer (LC) is declining in some countries, experts estimate that the global death rate will continue to rise in the near future, mainly due to an aging global population. By 2030, LC is expected to become the sixth most common cause of death, compared to its current position (the ninth most common cause of death) [1]. Currently, the localization of LC is the third most common type of cancer and is the most lethal type of cancer in the world [2]. In 2020, 98 886 new cases of cancer were reported in Romania, of which 12 122 (12.3%) were LC. Of these, the majority were men (9030 cases; 74.49%), and the rest were women (3092 patients; 25.5%). In male patients, LC was the most common location (16.8%), while in women this location was the fourth most common (6.8%) of neoplastic diseases, after breast cancer (26.9%), colon (11.8%) and cervix (7.5%) [3]. The number of LC deaths in 2020 in our country was 10 779, which is the highest prevalence rate of cancer-related deaths in Romania (19.8%) [1]. Symptoms of primary LC from the large bronchi are related to the degree of bronchial obstruction [4]. Patients with advanced central LC develop central airway obstruction (CAO) in 30% of cases [5]. This syndrome is manifested by severe dyspnea, hemoptysis, stridor, unilateral wheezing, atelectasis, post-stenotic pneumonia, severe respiratory failure, which in some cases requires assisted mechanical ventilation [6]. In present, flexible fiberoptic bronchoscopy (FFB) is the essential method for both the diagnosis and staging of central LC and for the therapeutic interventions necessary to restore airway permeability in patients with obstruction of the large airways and who have contraindications for surgery [7]. Since the first attempts to screen for this disease (2005), numerous studies have emerged in Europe, with early detection by genetic methods playing an important role [8].

Currently, in addition to implementing a healthy lifestyle, it is necessary to create national networks of bronchology, with a uniform territorial distribution, allowing access to all symptomatic people and at high risk of LC to specific diagnostic investigations [9]. To achieve this goal, it is necessary to set up a multidisciplinary team with experts in pneumology, imaging, oncology, thoracic surgery, pathology, family medicine and patient representatives [10]. Within this team, bronchologists and pathologists play the most important roles in the positive diagnosis of LC [11].

Aim

The main aim of the current study was to describe the main pathological forms of LC in the large airways and the presentation of their bronchoscopic aspects in a Romanian cohort of LC patients.

Patients, Materials and Methods

We conducted a retrospective clinical study of 38 patients who were hospitalized and diagnosed with LC in the Clinic of Pneumology, Victor Babeş Hospital for Infectious Diseases and Pneumology and Clinic of Thoracic Surgery, Emergency County Hospital, Craiova, Romania, from 2019 to 2020. The diagnosis of LC was established based on the anamnesis and the clinical evaluation, correlated with the biological and imagistic investigations, and confirmed by FFB of these patients. For the bronchoscopic examination, we used in the Department of Bronchology, Victor Babeş Hospital for Infectious Diseases and Pneumology, Craiova, an Olympus Evis Exera 160 system, consisting of CV-160 video processor, CLV-160 300 W Xenon light source, 19" high-definition medical monitor and BF-P160 video bronchoscope with 2 mm working channel and 4.9 mm external diameter. The forceps used to take the biopsies from the tumoral lesions were represented by the standard fenestrated FB-19C-1 and alligator FB-15C-1 models. The biopsied tumor tissue was suspended in recipients containing 10% neutral buffered formalin and sent immediately to the Laboratory of Histopathology within the Hospital. Endobronchial tumors were recorded during bronchoscopy and registered in our database for further correlation with HP results. The identified tumoral lesions were biopsied using the forceps listed above, the number of biopsies averaging 3–4, depending on the position of the tumor, biopsy-related bleeding, and tolerance of the procedure by the patient. All patients were subsequently monitored in the Department of Bronchology for approximately one hour, for further monitoring of vital signs and for early detection of certain complications. No patients presented significant complications during or after the procedure, which required additional measures or transfer to the Intensive Care Unit (ICU) located in the immediate vicinity. The bronchoscopies were performed with maximum safety and without notable incidents or accidents. Exclusion criteria were history of allergic disease, uncooperative patient, acute or recent myocardial infarction, unstable angina, severe respiratory failure with partial pressure of oxygen (PaO_2) levels less than 45 mmHg, coagulation disorders, severe asthma, active pulmonary tuberculosis, and superior vena cava syndrome.

HP investigations were performed on the specimen samples collected from the patients by bronchofibroscopy or after thoracotomy. The biopsy fragments of the lungs were processed by the classical histological technique with 24 hours routine 4% formalin fixation, and paraffin embedding in the Pathology Laboratories of the Victor Babeş Hospital for Infectious Diseases and Pneumology and of the Emergency County Hospital, Craiova. From the resulting paraffin blocks, 4 μm thick sections were cut at the microtome, then stained with Hematoxylin–Eosin (HE). The stained sections were examined under a Nikon Eclipse 55i microscope by two pathologists highlighting the lesions characteristic of LC. Imagistic investigations (thorax radiography, chest tomography) were made with equipment used by the Laboratory for Radiology and Medical Imaging from both Hospitals. Laboratory samples involving hematology, biochemistry, immunology, bacteriology, and gasometric methods) were done in the Clinical Laboratory of the Hospitals using the system known as Celltac Nihon Kohden and Vitros 250 dry chemistry analyzers. The statistical analysis was performed using the Microsoft Excel (Microsoft Corp., Redmond, WA, USA), together with the XLSTAT add-on for MS Excel (Addinsoft SARL, Paris, France) and IBM Statistical Package for the Social Sciences (SPSS) Statistics 20.0 (IBM Corporation, Armonk, NY, USA) for data processing. Because the numerical variables investigated had a normal data distribution, globally or in every studied group, we were allowed to use the parametric statistical tests (*e.g.*, Student's *t*-test) and the results were summarized as the mean value ± standard deviation. For all statistical tests, *p*-values less than 0.05 were considered significant. All hematological, biochemical, imagistic, and endoscopic investigations were made after obtaining the informed consent from the patients, which guarantees the fundamental rights of the patient.

Results

Demographic data

The group consisted of 32 (84.21%) men and six (15.78%) women. The mean age of patients diagnosed with LC was 64.63±6.07 years, with values ranging from 48 to 79 years. Over two-thirds of the patients (26 patients; 68.42%) lived in urban areas, and one third of them (12 patients; 31.57%) came from rural areas. Following the pathological examination, the patients were divided into two main groups, one group of patients with non-small cell lung cancer (NSCLC) and another of patients with small cell lung cancer (SCLC). The demographic characteristics and risk factors involved in the occurrence of LC in these patients are presented in Table 1.

Clinical data

The most common symptoms and clinical signs in patients with LC were chronic cough in 32 (84.21%) cases, followed by dyspnea in 24 (63.15%) cases, sputum in 23 (60.53%) cases, hemoptysis in 10 (26.31%) cases, weight loss in 22 (57.89%) cases, pallor in 22 (57.89%) cases, cyanosis in 21 (55.26%) cases, underweight in 18 (47.36%) cases, loss of appetite in 14 (36.84%) cases, fever in nine (23.68%) cases, and wheezing in two (5.26%) cases. The main complications of LC in the patients included in the

study were: obstructive pneumonia in nine (23.68%) patients, atelectasis in 16 (42.1%) patients and respiratory failure in 21 (55.26%) patients. Incidences of clinical manifestations and complications encountered in patients with the two pathological forms are reported in Table 2.

Table 1 – ***The demographic features and risk factors involved in the occurrence of various histological forms of LC***

	The group of patients with NSCLC	The group of patients with SCLC	LC patients
No. of patients [*n*] (%)	30 (78.94%)	8 (21.05%)	38 (100%)
Age [years]	66.33±5.15	58.25±6.81	64.63±6.07
Men [*n*] (%)	24 (80%)	8 (100%)	32 (84.21%)
Women [*n*] (%)	6 (20%)	0	6 (15.78%)
Urban [*n*] (%)	21 (70%)	5 (62.5%)	26 (68.42%)
Rural [*n*] (%)	9 (30%)	3 (37.5%)	12 (31.57%)
Active smokers [*n*] (%)	15 (50%)	6 (75%)	21 (55.26%)
Ex-smokers [*n*] (%)	10 (33.33%)	2 (25%)	12 (34.28%)
Non-smokers [*n*] (%)	5 (16.66%)	0	5 (13.1%)
COPD history [*n*] (%)	5 (16.66%)	2 (25%)	7 (18.42%)
Tuberculosis history [*n*] (%)	2 (6.66%)	1 (12.5%)	3 (7.89%)
Silicosis history [*n*] (%)	1 (3.33%)	0	1 (2.63%)

COPD: Chronic obstructive pulmonary disease; LC: Lung cancer; *n*: No. of patients; NSCLC: Non-small cell lung cancer; SCLC: Small cell lung cancer.

Table 2 – ***Incidence of clinical features and complications encountered in patients with the two pathological forms of LC***

Symptoms/ complications	Incidence of clinical manifestations in patients with NSCLC	Incidence of clinical manifestations in patients with SCLC	Statistical significance *p*-value
Cough [*n*] (%)	25 (83.33%)	7 (87.5%)	0.78
Dyspnea [*n*] (%)	20 (66.66%)	4 (50%)	0.39
Expectoration [*n*] (%)	19 (63.33%)	4 (50%)	0.50
Hemoptysis [*n*] (%)	8 (26.66%)	2 (25%)	0.92
Cyanosis [*n*] (%)	18 (60%)	3 (37.5%)	0.26
Pallor [*n*] (%)	20 (66.66%)	2 (25%)	0.05
Wheezing [*n*] (%)	1 (3.33%)	1 (12.5%)	0.31
Inappetence [*n*] (%)	10 (33.33%)	4 (50%)	0.39
Weight loss [*n*] (%)	17 (56.66%)	5 (62.5%)	0.77
Underweight [*n*] (%)	15 (50%)	3 (37.5%)	0.54
Fever [*n*] (%)	7 (23.33%)	2 (25%)	0.92
Obstructive pneumonia [*n*] (%)	7 (23.33%)	2 (25%)	0.92
Atelectasis [*n*] (%)	13 (43.33%)	3 (37.5%)	0.62
Respiratory failure [*n*] (%)	18 (60%)	3 (37.5%)	0.26

LC: Lung cancer; *n*: No. of patients; NSCLC: Non-small cell lung cancer; SCLC: Small cell lung cancer.

Biological data

The mean values of hematological and biochemical parameters recorded in patients with LC were hemoglobin (Hb) 12.68±1.32 (10–15 g/dL), white blood cell (WBC) count 9799±267 (4000–21500/mm^3), platelet (PLT) count 321.263±93.950 (112 000–768 000/mm^3), erythrocyte sedimentation rate (ESR) (1 h) 64.21±29.49 (7–130 mm/1 h), creatinine 0.89±0.15 (0.52–1.5 mg/dL), urea 24.36±8.24 (15–64 mg/dL), alanine aminotransferase (ALT) 25.07± 15.11 (7–155 U/L), prothrombin time (PT) 12.5±1.31 (11–14 s). The mean values of hematological and biochemical parameters recorded in patients in the two groups are shown in the Table 3.

Table 3 – ***Mean values and SDs of hematological and biochemical parameters recorded in patients in the two groups of LC***

	Mean value and SD of hematological and biochemical parameters recorded in patients with NSCLC	Mean value and SD of hematological and biochemical parameters recorded in patients with SCLC	Statistical significance *p*-value
Hb [g/dL]	12.5±1.3	13.37±1.18	0.16
WBC count [No./mm^3]	9436±2595	11 162±3128	0.43
PLT count [No./mm^3]	340 900±92 340	247 625±88 781	0.48
ESR [mm/1 h]	66.16±31.43	56.87±20.40	0.37
ALT [U/L]	24.83±16.01	26±11.5	0.21
PT [s]	12.66±1.51	11.87±0.65	0.51
BUN [mg/dL]	22.83±8.34	20.12±6.40	0.19
Creatinine [mg/dL]	0.89±0.16	0.87±0.12	0.18

ALT: Alanine aminotransferase; BUN: Blood urea nitrogen; ESR: Erythrocyte sedimentation rate; Hb: Hemoglobin; LC: Lung cancer; NSCLC: Non-small cell lung cancer; PLT: Platelet; PT: Prothrombin time; SCLC: Small cell lung cancer; SD: Standard deviation; WBC: White blood cell.

Imaging study

Chest radiography, the diagnostic imaging method initially used for the patients included in the study, revealed abnormal radiological features that suggested the diagnosis of bronchogenic carcinoma in 27 (90%) patients with NSCLC and five (62.5%) patients with SCLC. In three (10%) patients with NSCLC and three (37.5%) patients with SCLC, lung X-rays were normal. The radiological findings observed were enlargement of the pulmonary hilum in five (13.15%) patients, unique parenchymal opacity in 14 (36.84%) patients, multiple parenchymal opacities in four (10.52%) patients, atelectasis in five (13.15%) patients, persistent or recurrent pneumonic opacity in seven (18.42%) patients, pleural effusion in eight (21.05%) patients and focal pleural thickening in one (2.63%) patient. The radiological findings observed in chest X-ray are shown in the Table 4.

In patients with malignant tumors of the large airways who showed clinical manifestations and nonspecific radiological changes, chest computed tomography (CT) with contrast was the best non-invasive method for assessing these tumor lesions. In our patients, chest CT scan established a positive diagnosis of LC, by highlighting certain tomographic signs of certainty. Contrast-enhanced chest CT scan in 38 patients diagnosed with LC showed: iodophilic tumor formations in 37 (97.36%) patients, the appearance

of obstructive pneumonia in nine (23.68%) patients, and atelectatic condensation in 12 (31.57%) patients. Tumors were localized in the trachea in four (10.52%) cases, while parenchymal tumors were located in the right lung in 16 (42.1%) patients, and in the left lung in 17 (44.73%) patients. Contrast-enhanced chest CT could not visualize a tumor located in the middle lobe bronchus in a patient with NSCLC. Hilar and peribronchial lymphadenopathy were described in three (7.89%) patients, ipsilateral subcarinal and mediastinal lymphadenopathy were observed in 19 (50%) patients, and contralateral mediastinal lymphadenopathy was described in only 13 (34.21%) patients. Hilary, peribronchial, subcarinal and mediastinal lymphadenopathy were absent in six (15.78%) patients. Lung metastases were seen in three (67.89%) patients, while pleural effusion was present in 13 (34.21%) patients, and pleural thickening was in one (2.63%) patient. The CT findings observed in contrast-enhanced chest in patients with various histological types of LC are presented in the Table 5.

Table 4 – ***Radiological findings in patients with different histological types of LC***

Radiological findings	NSCLC	SCLC	LC
No. of patients [*n*] (%)	30 (78.84%)	8 (21.16%)	38 (100%)
Enlargement of the hilum [*n*] (%)	3 (10%)	2 (26%)	5 (13.15%)
Unique parenchymal opacity [*n*] (%)	12 (40%)	2 (25%)	14 (36.84%)
Multiple parenchymal opacities [*n*] (%)	2 (6.66%)	2 (25%)	4 (10.52%)
Pleural effusion [*n*] (%)	8 (26.66%)	0 (0%)	8 (21.05%)
Atelectasis [*n*] (%)	3 (10%)	2 (25%)	5 (13.15%)
Pneumonic opacity [*n*] (%)	5 (16.66%)	2 (25%)	7 (18.42%)
Pleural thickening [*n*] (%)	0	1 (12.5%)	1 (2.63%)
Normal radiological [*n*] (%)	3 (10%)	3 (37.5%)	6 (15.78%)

LC: Lung cancer; NSCLC: Non-small cell lung cancer; SCLC: Small cell lung cancer.

Table 5 – ***CT findings in 38 patients with various histological types of LC patients***

Thoracic findings	NSCLC	SCLC	LC
No. of patients [*n*]	30 (78.84%)	8 (21.16%)	38 (100%)
Tracheal tumor [*n*] (%)	3 (10%)	1 (12.5)	4 (10.52%)
Iodophilic parenchymal tumor [*n*] (%)	26 (86.66%)	7 (87.5%)	32 (84.21%)
Right lung tumor [*n*] (%)	13 (43.33%)	3 (62.5%)	16 (42.1%)
Left lung tumor [*n*] (%)	13 (43.33%)	4 (37.5%)	17 (44.73%)
Absence of tumor formation [*n*] (%)	1 (3.33%)	0	1 (2.63%)
Pneumonic condensation [*n*] (%)	7 (23.33%)	2 (25%)	9 (26.68%)
Atelectatic condensation [*n*] (%)	9 (30%)	3 (37.5%)	12 (31.57%)
Unilateral hilar and peribronchial lymphadenopathy [*n*] (%)	2 (6.66%)	1 (12.5%)	3 (7.89%)
Ipsilateral subcarinal and mediastinal lymphadenopathy [*n*] (%)	16 (53.33%)	3 (25%)	19 (50%)
Contralateral mediastinal lymphadenopathy [*n*] (%)	10 (33.33%)	3 (62.5%)	13 (34.21%)
Absence of lymphadenopathy [*n*] (%)	2 (6.66%)	1 (12.5%)	3 (7.89%)
Lung metastases [*n*] (%)	2 (6.66%)	1 (12.5%)	3 (7.89%)
Pleural effusion [*n*] (%)	13 (43.33%)	0	13 (34.21%)
Focal pleural thickening [*n*] (%)	0	1 (12.5%)	1 (2.63)

CT: Computed tomography; LC: Lung cancer; NSCLC: Non-small cell lung cancer; SCLC: Small cell lung cancer.

Tumor, node, metastasis (TNM) staging of patients with NSCLC based on bronchofibroscopy and chest CT showed: stage II in three (10%) patients, stage III in 12 (40%) patients and stage IV in 15 (50%) patients. The SCLC staging performed by the same imaging and morphological diagnostic methods, revealed localized disease in three (37.5%) patients and advanced disease in five (62.5%) patients.

The bronchoscopy studies

The most frequent location of the lung tumors was the left main bronchus (11 patients; 28.94%). The location of LC for the other patients included in the study is reported in Table 6. The endoscopic aspects of the tumor lesions were infiltrating lesion in 21 (55.26%) patients (Figure 1A), exophytic or mass endobronchial lesion in eight (21.05%) patients (Figure 1B) and mixed lesion (exophytic and infiltrating lesion) in seven (18.42%) patients (Figure 1C). The examination could not visualize two (5.26%) tumors localized in the right lower lobe bronchus in a patient with NSCLC and in the left upper lobe (LUL) in a patient with SCLC. In both cases, extrinsic compression was important (tumor atelectasis) such that the tumor could not be accessed by bronchoscopic examination. Extrinsic compression of the bronchial wall was described in 18 (47.36%) of the bronchoscopically evaluated patients.

Table 6 – ***Bronchofibroscopic findings in the 38 patients with different histological types of LC***

Bronchofibroscopic findings		NSCLC	SCLC	LC
Tumor findings [*n*] (%)		30 (78.94%)	8 (21.05%)	38 (100%)
Location [*n*] (%)	*Tracheal*	1 (3.33%)	1 (14.28%)	2 (5.26%)
	Tracheobronchial	2 (6.66%)	0	2 (5.26%)
	RMB	5 (16.66%)	1 (14.28%)	6 (15.78%)
	LMB	10 (33.33%)	1 (14.28%)	11 (28.94%)
	RUL	4 (13.33%)	2 (28.57%)	6 (15.78%)
	ML	2 (6.66%)	0	2 (5.26%)
	RLL	2 (6.66%)	0	2 (7.89%)
	LUL	3 (10%)	2 (28.57%)	5 (13.15%)
	LLL	1 (3.33%)	0	1 (2.63%)
Macroscopic appearance [*n*] (%)	*Infiltrating tumor*	16 (53.33%)	5 (71.42%)	21 (55.26%)
	Exophytic (mass)	7 (23.33%)	1 (14.28%)	8 (21.05%)
	Infiltrative-exophytic (mixed)	6 (20%)	1 (14.28%)	7 (18.42%)
	Undetected tumor	1 (3.33%)	1 (14.28%)	2 (5.26%)
Extrinsic compression [*n*] (%)		14 (46.66%)	4 (50%)	18 (47.36%)
Incomplete bronchial stenosis [*n*] (%)		17 (56.66%)	5 (62.5%)	22 (57.89%)
Atelectasis [*n*] (%)		13 (43.33%)	3 (37.5%)	16 (42.10%)
The mechanism of bronchial stenosis [*n*] (%)	*Endoluminal*	15 (50%)	4 (50%)	19 (50%)
	Mixed	9 (30%)	3 (37.5%)	12 (31.57%)
	Extraluminal	6 (20%)	1 (12.5%)	7 (18.42%)

Bronchofibroscopic findings		NSCLC	SCLC	LC
Bronchial mucosa [*n*] (%)	*Normal*	9 (30%)	2 (25%)	11 (28.94%)
	Pale and atrophied	9 (30%)	3 (37.5%)	12 (31.57%)
	Erythematous and edematous	12 (40%)	3 (37.5%)	15 (39.47%)
Bronchial secretions [*n*] (%)		8 (26.66%)	2 (25%)	10 (26.31%)
Bronchiectasis [*n*] (%)		2 (6.66%)	2 (25%)	4 (10.52%)

LC: Lung cancer; LLL: Left lower lobe; LMB: Left main bronchus; LUL: Left upper lobe; ML: Middle lobe; *n*: No. of patients; NSCLC: Non-small cell lung cancer; RLL: Right lower lobe; RMB: Right main bronchus; RUL: Right upper lobe; SCLC: Small cell lung cancer.

The tumor lesions caused a narrowing (partial or significant stenosis) of the bronchial lumen in 22 (57.89%) patients and a complete obstruction (atelectasis) in 16 (42.10%) patients. Atelectasis was described in the main bronchi in three (18.75%) cases, in the lobar bronchi in 12 (75%) and in the segmented bronchi in one case (6.25%). Malignant bronchial stenosis was achieved by endoluminal mechanism in 19 (50%) patients, by mixed mechanism in 12 (31.57%) patients and by extraluminal mechanism in seven (18.42%) patients (Figure 2, A–C).

Bronchoscopically, the mucosa of the bronchial tree was normal in 11 (28.94%) patients, pale and atrophied in 12 (31.57%) patients, erythematous and edematous in 15 (39.47%) patients, bronchial secretions were reported in 10 (26.31%) patients, and bronchiectasis was described in four (10.52%) patients. The bronchoscopic findings observed in the 38 patients with different histological types of LC patients are presented in Table 6.

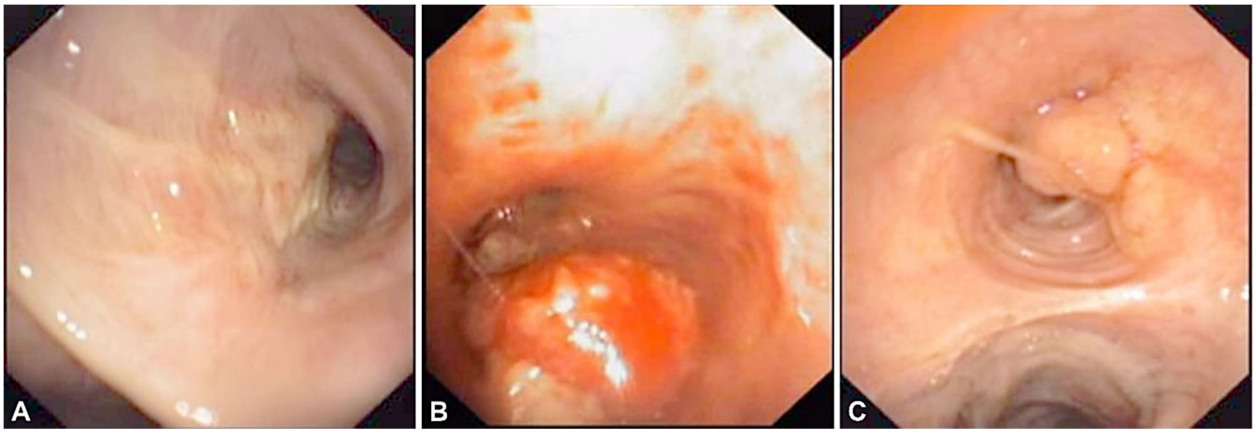

Figure 1 – ***Macroscopic aspects of tracheobronchial tumors highlighted bronchoscopically: (A) Infiltrative tumor, with irregular surface, at the level of the posterior wall of the left primitive bronchus; (B) Exophytic tumor, well vascularized, with irregular surface, which obstructs the right basal pyramid; (C) Mixed tumor (infiltrative-exophytic) located at the level of the anterior wall of the left upper lobe bronchus.***

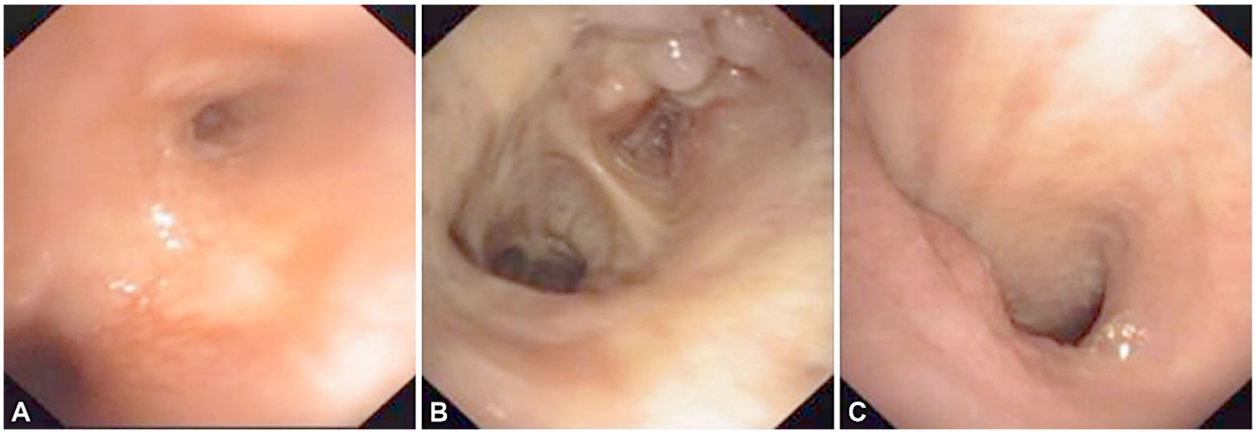

Figure 2 – ***Bronchoscopic aspects of malignant bronchial stenoses encountered in the studied patients: (A) Malignant bronchial stenosis due to extrinsic compression and malignant infiltration of the mucosa on the LUL bronchus; (B) Significant malignant stenosis of the LUL bronchus by polylobate infiltrative tumor and extrinsic compression; (C) Partial tracheal stenosis due to the presence of irregular, well-vascularized infiltrative tumor, and extrinsic compression. LUL: Left upper lobe.***

The pathological study

The pathological exam of small fragments from bronchial biopsies and tissue fragments obtained through the surgical specimen section revealed microscopic aspects specific to squamous cell carcinoma (SCC) in 19 (50%) patients, adenocarcinoma (ADC) in 11 (28.94%) patients and SCLC in eight (21.06%) patients.

The main lesions specific to SCC, which allowed the diagnosis of this form of LC were sheets or lobules composed of polygonal malignant cells with eosinophilic cytoplasm and pleomorphic nuclei, with atypical mitosis; the existence of keratosis pearls (Figure 3A); the presence of intercellular junctions (Figure 3B). In the case of undifferentiated SCC, polygonal or rounded malignant cells were observed, without a tendency to keratinize or to form

keratotic pearls, usually with marked nuclear pleomorphism and frequent atypical mitosis.

In the case of pulmonary ADC, the malignant polygonal cells were arranged in the form of pseudoglands or tubes, of various shapes and sizes, with obvious nuclear pleomorphism and the presence of typical and atypical mitoses. These cells may produce mucin. ADCs can have a great HP diversity, being described five distinct types: (*i*) lepidic, in which tumor cells proliferate along the pre-existing alveolar structures (Figure 3C); (*ii*) acinar, in which the tumor proliferation achieves a dominant glandular pattern, with round/oval malignant glands invading the fibrous stroma (Figure 3D); (*iii*) papillary, in which the cuboidal and columnar tumor cells replace the alveolar delimiting epithelium and which also line the conjunctivo-vascular axes projected in the alveolar lumen; (*iv*) micropapillary, in which malignant cells proliferate in the form of cellular "clusters", most of which do not show fibrovascular cores; (*v*) solid with mucin, in which malignant cells proliferate in the form of superimposed cell layers.

In SCLC, round, oval, or spindle-shaped tumor cells were small (usually less than three times the diameter of small lymphocytes), with reduced cytoplasm, and ill-defined cytoplasmic borders (Figure 3E). The nuclei were hyperchromatic, with finely dispersed granular chromatin ("salt and pepper" appearance) and absent nucleoli (Figure 3F). Mitotic activity was increased, and necrosis was common. Nuclear molding is a constant aspect. In small biopsy specimens, SCLC nuclei usually showed elongation crushing, agglomeration, and diffusion of chromatin material.

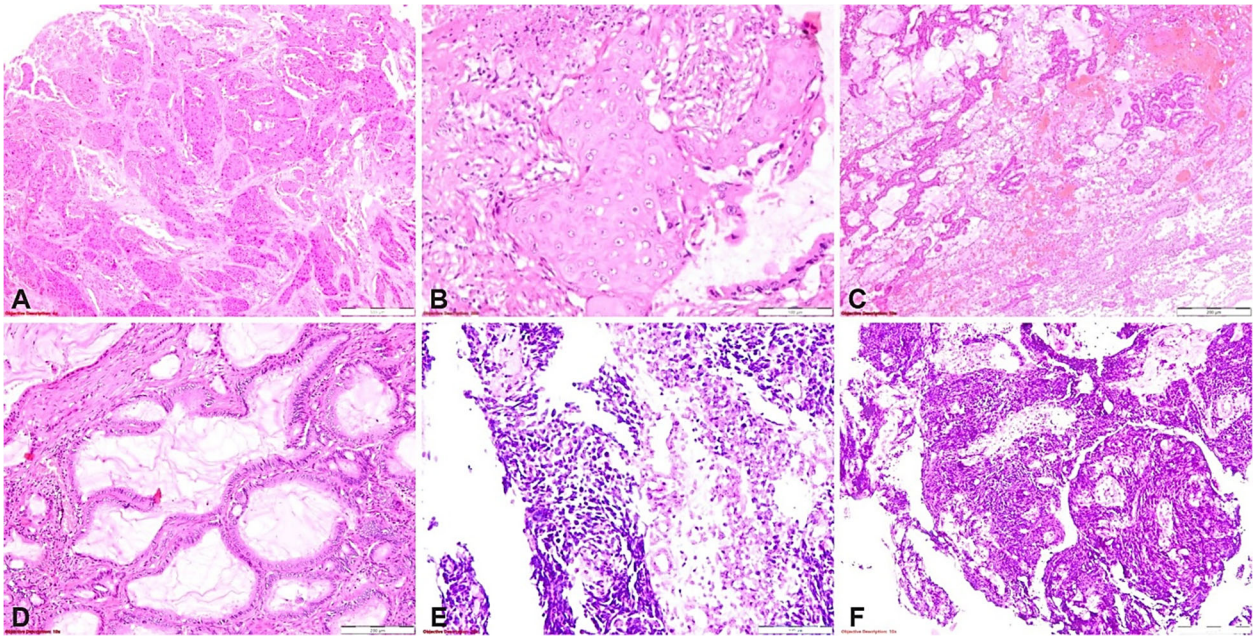

Figure 3 – ***Microscopic aspects encountered in the studied patients: (a) Well-differentiated lung SCC composed of sheets or islands of large polygonal malignant cells containing keratin, and with the presence of keratin pearls in the center of neoplastic proliferations; (B) Lung SCC – invasive island of large polygonal malignant cells containing keratin and intercellular bridges; (C) Lung invasive mucinous ADC with lepidic (in situ) and acinar tumor growth pattern and intra-alveolar mucin and hemorrhagic areas; (D) Lung invasive mucinous ADC with acinar tumor growth pattern and intra-alveolar mucin predominantly composed of cuboidal mucin-producing cells with eosinophilic cytoplasm; (E) SCLC consisting of sheets and clusters of small to medium sized, round to oval blue neoplastic cells with minimal cytoplasm; (F) SCLC composed of small to medium sized, round to oval blue neoplastic cells with minimal cytoplasm and nuclei, with no distinct nucleoli. HE staining: (A, C and E) ×40; (D) ×100; (B and F) ×400. ADC: Adenocarcinoma; HE: Hematoxylin–Eosin; SCC: Squamous cell carcinoma; SCLC: Small cell lung cancer.***

The morphological study

The concomitant analysis of the macroscopic and microscopic findings of the lung tumors diagnosed by FFB allowed the establishment of endoscopic features for the three pathological types of bronchial tumors discovered in our patients.

SCC was the most common pathological form in our study, being identified in 19 (50%) patients. The FFB in white light identified the presence of the tumor lesions in the distal trachea with interest in carina in two (10.52%) patients, in the main bronchi in 13 (68.42%) patients and in the lobar bronchi in four (21.05%) patients. The endobronchial findings of the lung tumors were infiltrating or invasive lesions in 14 (73.68%) patients (Figure 4A), endoluminal mass in three (15.78%) patients and mixed in two (10.52%) patients. Extrinsic compression of the bronchial wall has been described in seven (36.84%) patients (Figure 4B). The tumor lesions caused partial or significant narrowing of the bronchial lumen in 11 (57.89%) patients and atelectasis in eight (42.11%) patients. Atelectasis was described in the main bronchi in one (5.26%) case and in the lobar bronchi in seven (36.84%) patients (Figure 4C). The mechanisms of malignant bronchial obstruction were: endoluminal in 11 (31.57%) patients and mixed (combined endo- and extraluminal) in eight (42.10%) patients. Regarding the appearance of the airway mucosa, the erythematous and edematous appearance was highlighted in nine (47.36%) patients, the atrophy and pale appearance in seven (36.84%) patients, and the normal appearance in five (26.31%) patients. Bronchial secretions were observed in five (26.31%) patients, and the bronchiectasis was present in only one (5.26%) patient.

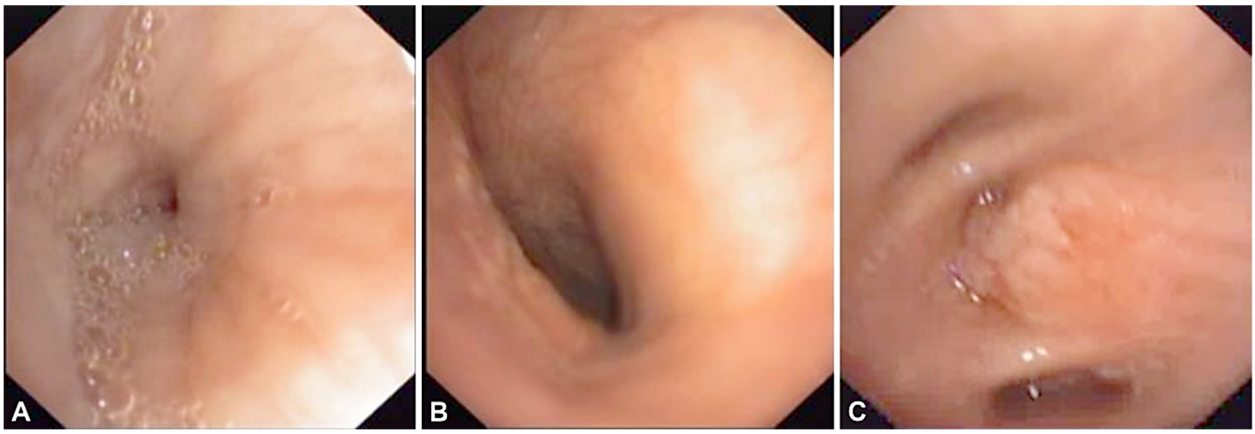

Figure 4 – ***Bronchoscopic aspects of squamous cell carcinomas (WL mode): (A) Concentric infiltrative tumor and extrinsic compression that produce punctiform stenosis of the left lower apical segmental bronchus at onset; (B) Tracheal stenosis due to irregular, well-vascularized infiltrative tumor, located on the right lateral wall and extrinsic compression; (C) Malignant atelectasis of the lateral segmental bronchus of the right basal pyramid by extrinsic compression and vegetative, nodular, well-vascularized tumor. WL: White light.***

ADC was the second most prevalent HP form in our group of patients with LC. The bronchoscopic examination revealed an exophytic lesion or mass in the trachea in one (9.09%) patient, in the main bronchi in two (18.18%) patients and in the lobar bronchi in seven (63.63%) patients. In one patient (9.09%), the infiltrating lesion was highlighted in the lower right lobe bronchus after surgery. The macroscopic aspect of the tumor formations was: endoluminal mass in four (36.36%) patients (Figure 5A), infiltrating lesion in two (18.18%) patients, mixed in four (36.36%) patients, and could not be highlighted due to extrinsic parietal compression in one (9.09%) case. Extrinsic bronchial compression was observed in two (18.18%) patients. Malignant bronchial stenosis (narrowing of the bronchial lumen) was found in six (54.54%) patients (Figure 5B), and malignant atelectasis in five (45.45%) patients. The site of atelectasis was found in the main bronchi in two (18.18%) patients and in the lobar bronchi in three (26.31%) patients (Figure 5C). Malignant bronchial obstruction was the consequence of the endoluminal mechanism in nine (81.81%) patients, extraluminal in one (9.09%) patient and mixed in one (9.09%) patient. The changes in the bronchial mucosa described in these patients were: erythematous and edematous appearance in four (36.36%) patients, atrophy, and pale appearance in two (18.18%) patients. The mucosa was normal in five (45.45%) patients. Bronchial secretions were mentioned in three (27.27%) patients, and bronchiectasis was recognized in one (9.09%) patient.

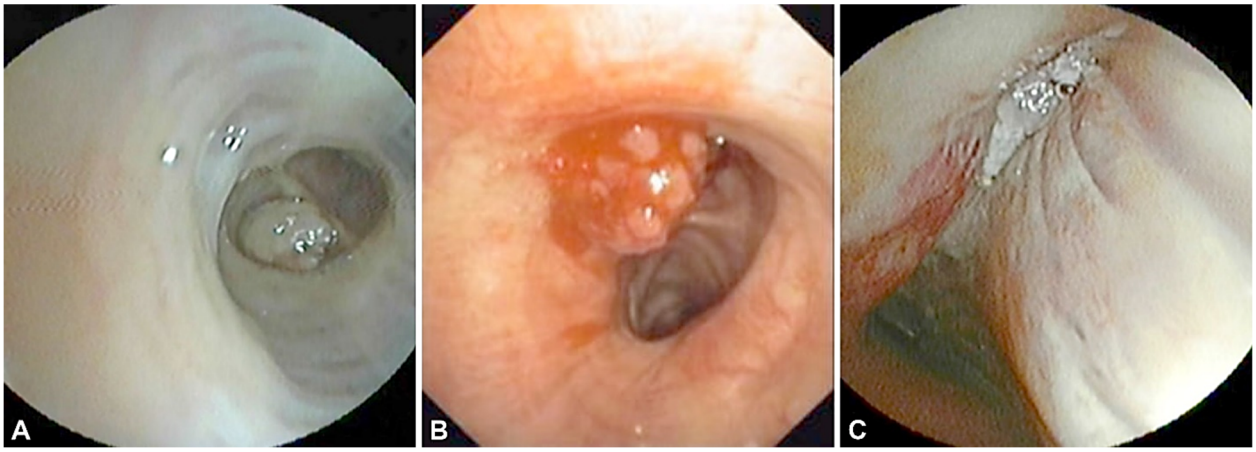

Figure 5 – ***Bronchoscopic aspects of adenocarcinomas: (A) Small nodular tumor, regular surface, pearly white, polypoid, significantly obstructing a subsegmentation of the left basal pyramid (LCI mode); (B) Bronchial malignant stenosis due to vegetative tumor, irregular surface, well-vascularized, sessile, with implantation base at the level of the posterior wall of the left primitive (WL mode); (C) Total right upper lobe atelectasis by extrinsic compression and vegetative tumor with surface necrosis (LCI mode). LCI: Linked color imaging; WL: White light.***

SCLC was identified in only eight (21.05%) of the investigated patients. The FFB found the tumor lesions at the level of trachea in one (12.5%) case, main bronchi in two (25%) cases and lobar bronchi in four (50%) cases. Bronchial tumor lesion could not be visualized by bronchofibroscopy in one (12.5%) case, due to extrinsic bronchial compression, in which case the diagnosis of upper left lobar infiltrating lesion was established following surgery. Macroscopically, the tumor formations had an infiltrating finding in five (62.5%) of the patients diagnosed with SCLC (Figure 6A), endobronchial mass in one (12.5%) of the patients (Figure 6B) and mixed finding in one (12.5%) patient. Extrinsic compression of the affected bronchus was described in three (37.5%) of the bronchoscopically examined patients. The tumor lesions resulted in a malignant stenosis (partial or important narrowing) of the bronchial

endolumen in five (62.5%) patients and malignant atelectasis in three (37.5%) patients (Figure 6C). The site of atelectasis was in the lobar bronchi in two (25%) patients and segmental in one (12.5%) patient. Malignant bronchial obstruction was achieved by mechanisms: endoluminal in five (62.5%) of patients, mixed in two (25%) patients and extraluminal in one (12.5%) patient. The appearance of the tracheobronchial mucosa was atrophy and pale in three (37.5%) patients, edematous and erythematous in two (25%) patients and normal in one (12.5%) patient. Pathological endobronchial secretions and bronchiectasis of the bronchial wall have been described in two (25%) patients.

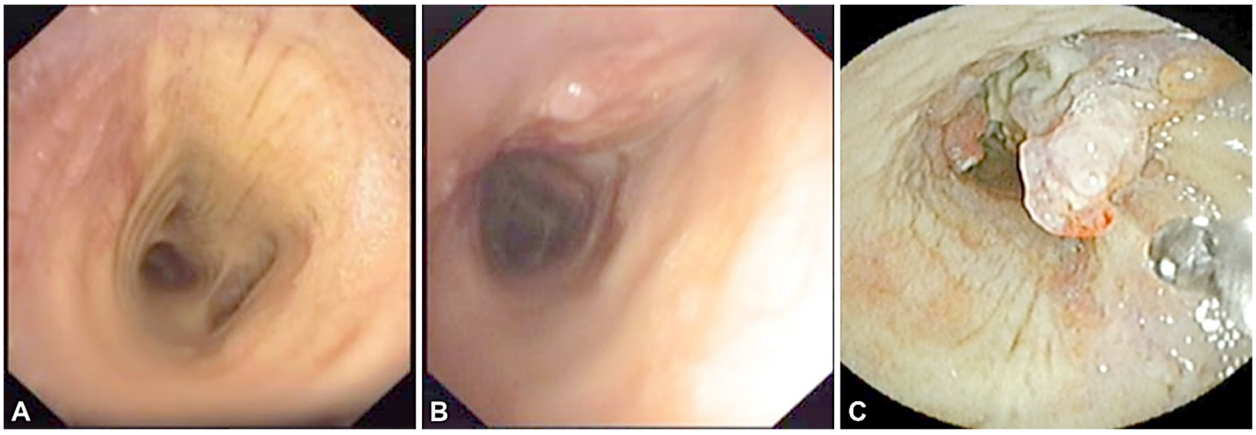

Figure 6 – ***Bronchoscopic aspects of small cell carcinomas: (A) Small nodular tumor, sessile, on the background of an irregularly infiltrated mucosa, at the level of the posterior wall of the right distal primitive (WL mode); (B) Infiltrative tumor, irregular surface, well-vascularized, at the level of the right lateral wall of the middle portion of the trachea; (C) Total right upper lobe atelectasis by well-vascularized polylobate exophytic tumor protruding into the lumen of the right primitive (LCI mode). LCI: Linked color imaging; WL: White light.***

Discussions

The epidemiological study

The main risk factors for LC identified among the patients included in our study were: old age, male sex, urban environment, smoking status, personal history of chronic obstructive pulmonary disease (COPD), pulmonary tuberculosis, and silicosis. The median age of the patients diagnosed with LC was 66 years, being lower than the median age found by Daneshvar *et al.* on a group of 342 patients with LC (72 years) [12]. In our study, the median age found in the patients with NSCLC (66 years) was significantly higher than the median age of the patients with SCLC (56 years). In general, men have a higher predisposition to develop LC than women [13]. In our study, many patients were men (84.21%), both in the group of patients with NSCLC and among patients with SCLC. Over the past two decades, the ratio between men and women diagnosed with this disease has changed dramatically, with the incidence observed to be decreasing in men, but continuing to increase in women in several regions of the world [14]. Over two-thirds of the patients enrolled in this study came from urban areas (68.42%). According to a study conducted by Paquette & Finlayson on a group of 161 479 newly diagnosed LC patients, most of them came from urban areas. The authors developed a model of ordinary logistic regression by which they demonstrated that age, background, race, sex, marital status, income level and level of education correlated with the late stage of the disease at the time of presentation [15]. The most common comorbidity encountered in our LC patients was COPD. In this study, seven (18.42%) patients had a history of COPD. Miret *et al*. found a prevalence of COPD of 15.1% in the NSCLC patients with and 13.3% in the SCLC patients [16], similar to the results of our study, in which 16.66% of those with NSCLC and 25% of those with SCLC also had COPD. In the literature, COPD is a comorbidity commonly found in the LC patients, with a prevalence ranging from 40% to 70%, according to the used diagnostic criteria [17]. Another risk factor for the occurrence of LC was pulmonary tuberculosis. In our study, two (6.66%) NSCLC patients had a history of pulmonary tuberculosis and only one SCLC patient (12.5%) also had pulmonary tuberculosis history. A Chinese study conducted on 782 NSCLC patients revealed tuberculosis in the anamnesis of 64 (8.18%) patients [18]. Silicosis, one of the most common occupational diseases in the world, is an independent risk factor for LC in a percentage of up to 18%. In our study, the prevalence of silicosis in the LC patients' group was 2.63%, a result consistent with the conclusions of other studies [19].

The clinical study

The most important survival factor in the LC patients is the stage of the disease at the time of diagnosis. Also, in asymptomatic patients who are diagnosed by chance survival is much better compared to symptomatic patients. Unfortunately, most symptomatic patients have advanced disease at the time of diagnosis [20]. In our study, the clinical presentation was dominated by numerous symptoms and clinical signs, with variable incidences, whose were similar to that reported in the literature for: cough (8–75%) [21], dyspnea (3–60%) [22], expectoration (70–78%) [23], hemoptysis (6–35%) [21], weight loss (0–68%) [24], pallor (0–31.6%) [25], cyanosis (22.7%) [26], lack of appetite (57–61%) [20], chest pain (20–49%) [20], fever (0–20%) [23], and wheezing (0–2%) [27]. The comparative analysis of the incidence of the symptoms and clinical signs encountered in the two LC patients' groups showed no statistically significant differences for most of the clinical features encountered. However, in the NSCLC patients,

we encountered pallor (p=0.05) more frequently compared to the SCLC patients. The main complications in LC patients were obstructive pneumonia (23.68%), atelectasis (42.1%) and respiratory failure (55.26%). Although no statistically significant differences were observed between the incidences of the three complications in the two patient groups, higher incidences of atelectasis (43.33% *vs.* 37.5%) and respiratory failure (60% *vs.* 37.5%) were recorded in the NSCLC patients. In the literature, there are numerous studies in which the incidence of the three complications is variable, showing incidence of 24.6–44.9% for obstructive pneumonia [28, 29], 51.8% for atelectasis [25] and 51.8% for respiratory failure [30].

The laboratory findings

The comparative analysis of the average values of the studied hematological and biochemical parameters in the two groups of patients with LC showed no statistically significant differences between the average values of the two groups. However, anemia was more common in the patients with NSCLC (70%) compared to the patients with SCLC (25%), leukocytosis was more common in the patients in the group of those with SCLC (75%), compared to those in the group with NSCLC (43.33%), thrombocytosis was a more common hematological change in patients with NSCLC (56.66%), compared to patients with SCLC (25%), and elevated ESR levels were found in all patients with SCLC and in 90% of patients with NSCLC. The other clinical studies in patients with LC have shown that anemia [31], leukocytosis [32], and thrombocytosis [32] are negative prognostic factors in these patients. The average ERS values recorded in the studied patients were slightly higher than those found in other studies [33], with the mention that the patients with NSCLC showing higher average values. Elevated ALT levels were more frequently found in the patients with SCLC (25%) than in those with NSCLC (16.66%), that was also revealed by other international studies. In one of these studies was shown that high ALT levels did not correlate with a negative prognosis of these patients [34]. In the patients enrolled in our study, the average values of PT were normal (12.5±1.31 s), without observing statistically significant differences between the patients of the two groups of patients. The results of other studies, in which elevated average values of the PT were highlighted, revealed that the prolongation of the PT along with the increase in fibrinogen and D-dimer values was associated with an unfavorable prognosis in the studied patients [35]. Unlike the liver tests, elevated urea and creatinine levels were more common in the patients diagnosed with NSCLC (16.66%), compared to those with SCLC (11.11%). Elevated renal test levels were also found in patients of other clinical trials, without these elevated values being negative prognostic criteria [34].

The imaging study

Chest X-ray was the first investigation performed on a patient suspected of having LC. Although it is a useful imaging tool for providing preliminary information, it is not useful in characterizing and staging the disease [36]. In our study, chest radiographs revealed abnormal radiological features that suggested the diagnosis of bronchogenic carcinoma in most patients, in 32 (84.21%) patients. The comparative analysis of the pathological radiological aspects according to the pathological type of the malignant tumors showed statistically significant differences only in the case of opacity that suggested pleural effusion (21.05% *vs.* 0%), present only in patients with NSCLC. The incidences of the pathological aspects highlighted on the chest radiographs of the 104 patients diagnosed with lung neoplasm and evaluated by Sharma *et al.* were single parenchymal opacity (26.92%), multiple parenchymal opacity (8.65%), atelectasis (26.92%), pneumonic opacity (18.27%), homogenous latero-basal opacity (10.58%), mediastinal enlargement (3.85%), parenchymal cavities (8.65%), diaphragmatic paralysis (9.62%), rib involvement (7.69%) and pericarditis (3.86%) [37]. The comparative analysis of the pathological tomographic aspects encountered with predilection in the two groups of patients with LC showed that the presence of the tumor was demonstrated in 96.78% of patients with NSCLC and in all patients with SCLC. The location of the tumor in both lungs was equally distributed in patients with NSCLC and predominantly in the left lung in patients with SCLC. Impairment of the ipsilateral and precarinal mediastinal lymph nodes was more common in those with NSCLC than in those with SCLC, while mediastinal invasion, involvement of the hilar, peribronchial, and contralateral mediastinal lymph nodes were more commonly seen in patients with SCLC than in those with NSCLC. In patients with NSCLC, metastasis occurred predominantly in the pleura, while in patients with SCLC, metastasis occurred predominantly in the lungs and other organs. These results were consistent with those observed in other clinical studies regarding tumor identification [25], tumor location [25], presence of atelectasis [38], pleural metastasis [39–41], and distant metastasis [42–45]. On the other hand, the results regarding the pathological imaging aspects related to the presence of obstructive pneumonia [46] and mediastinal lymphadenopathy [25] were discordant with the results obtained by other authors. The Japanese study conducted by Kohno *et al.* showed a higher incidence of obstructive pneumonia in patients with SCLC compared to those with NSCLC (33.6% *vs.* 21.9%) [46]. If in our study the incidence of involvement of the ipsilateral pre-carinary or mediastinal lymph nodes in patients with LC was more frequent than that of the hilar or peribronchial lymph nodes (50% *vs.* 7.89%), in the clinical study performed by Alamoudi an approximately equal incidence of lymph node involvement was observed peribronchial or hilar and mediastinal or precarinal (30.7% *vs.* 38.6%) [25]. Based on the imaging and pathological results, the pre-therapeutic staging of the 38 patients was performed. In the case of patients with NSCLC, most patients were stage IV (50%), the rest being classified in stage III (40%) and stage II (10%). It was observed that most patients had an advanced stage of the disease (stage III and IV; 90%) and received only concomitant chemo- and radiotherapy treatment with concurrent chemoradiotherapy (CCRT), while only 10% could benefit from curative (surgical) treatment. Similar results, in which only 30% received surgical treatment, were published in a Chinese study [47]. Regarding patients with SCLC, the majority (62.5%) had extended disease (ED), and the rest (37.5%) were classified with limited disease (LD). In general, patients with LD should be offered concomitant chemo- and radiotherapy,

and those with ED should be offered palliative chemotherapy, as Alvarado-Luna & Morales-Espinosa mentioned in their review [48].

The bronchoscopic study

The FFB revealed the tumor, its exact location, the appearance of the tumor process, the degree of bronchial obstruction, the mechanism of production of malignant bronchial stenosis and the appearance of the bronchial mucosa. However, the most important aspect was the collection of a small fragment of the bronchial formation, which was subsequently analyzed by morphopathological examination.

The tracheal location of the tumor lesion was found in an equal proportion in both patients with NSCLC (10%), especially in the distal trachea, and in patients with SCLC (12.5%). Most tracheobronchial tumors affecting the distal trachea and carina have been shown to be NSCLC, especially SCC [49, 4]. Impairment of the right main bronchus (RMB) and right lung has been more commonly seen in patients diagnosed with NSCLC compared to diagnosed with SCLC (46.66% *vs.* 37.5%), while damage to the left main bronchus (LMB) and left lung were noted predominantly in those with SCLC compared to those with NSCLC (50% *vs.* 43.33%). The predominant damage to the right lung in patients with NSCLC was also observed in Jia's study, which also showed that tumors of the right lung had a more unfavorable prognosis than the evolution of tumors located in the left lung [50]. Frequent location of tumors the SCLC type in the left lung was also observed by Demetrian *et al*. in their study [51]. The tumors were mainly localized in the main bronchi in cases diagnosed with NSCLC, compared to those diagnosed with SCLC (50% *vs.* 25%), while lobar bronchial involvement was more common in cases with SCLC, compared to patients diagnosed with NSCLC (50% *vs.* 36.66%). In patients with NSCLC, especially in SCC, the preferred location of tumors was in the primary bronchi [52], while in patients with SCLC the location was predominant in the lobar and segmental bronchi [53]. The exophytic (mass tumor) and infiltrative-exophytic (mixed) aspects of bronchial tumors were more common in patients with NSCLC, compared to patients with SCLC (23.33% *vs.* 14.28%, respectively 20% *vs.* 14.28%). The infiltrative (infiltrating) lesion was the most common macroscopic tumor aspect in patients with SCLC (71.42%), compared to patients with NSCLC (53.33%). Similar incidences of major macroscopic type of lung tumor were described in a bronchoscopic study performed by Olaru *et al.* in 2013 [54]. Endobronchial tumors caused partial or significant stenosis in both NSCLC patients (56.66%) and SCLC patients (62.5%). Atelectasis was reported in 43.33% of patients with NSCLC and in 37.5% of those with SCLC. Obstructive lobar atelectasis, followed by collapse of lung tissue, occurred more frequently in patients with NSCLC in centrally located tumors [55–57]. In patients with NSCLC, atelectasis was observed in both the main bronchi (23.07%) and lobar bronchi (76.92%), while in patients with SCLC atelectasis was found in the lobar bronchi (66.6%) and the segmental ones (33.33%). Tracheobronchial malignancy is a life-threatening condition that can cause recurrent infections due to pulmonary atelectasis. Malignancies of the central respiratory tract can be mild, such as coughing and exertional dyspnea, but are often severe, leading to resting dyspnea, hemoptysis, post-obstructive infections, and asphyxiation [58, 59]. In LC of the central airways, malignant central airways obstruction is classified as extraluminal (extrinsic), endoluminal (intrinsic) or mixed (combined intrinsic and extrinsic) [6]. In our patients with NSCLC, malignant bronchial stenosis was achieved predominantly by endoluminal mechanism (50%), while mixed and extraluminal mechanisms were involved in 30% and 20% of the analyzed cases, respectively. In the cases with SCLC, the involvement of the three mechanisms in the production of malignant bronchial stenosis was represented as follows: endoluminal mechanism in 50% of cases, mixed in 37.5% and extraluminal in 12.5% of the examined cases. In patients with SCLC, the most aggressive subtype of LC, airway stenting has been reported to be helpful in patients with malignant stenosis of the airway [60]. Regarding the appearance of the airways' mucosa, patients with NSCLC presented a normal appearance of the mucosa more frequently than those with SCLC (30% *vs.* 25%) and the erythematous and edematous appearance of the mucosa (40% *vs.* 37.5%), while patients with SCLC had a higher incidence of atrophied appearance in the bronchial mucosa than those with NSCLC (37% *vs.* 30%). Bronchiectasis was observed more often in patients diagnosed with SCLC than in those diagnosed with NSCLC (25% *vs.* 6.66%), while bronchial secretions were reported in a similar percentage in the two groups of patients (26.66% of those with NSCLC and 25% of those with SCLC). The association of bronchial changes in the bronchial mucosa and bronchiectatic parietal lesions in most patients with LC has led a number of authors to consider that chronic inflammatory airway disease characterized by abnormal and permanent dilation of the bronchi, accompanied by high levels inflammatory cytokines [61], may be a risk factor for LC [13, 62–65].

The morphological study

In our studied cases, within the central airways, the dominant pathological form was SCC (71.42%). The literature mentions that the most SCC (70%) develop as lung tumors located in the central airways [66]. At the level of the lobar bronchi, in our patients, most cases showed pathological appearance of ADC (47.05%). The most majority of authors stated that ADC can evolve into single or multiple tumors [67] with varying sizes, most often peripherally located, in the vicinity of the pleura [68]. Nonetheless, the endobronchial aspects of the ADC located in the central respiratory tract are presented in several articles. In some cases, endobronchial ADC occurs as a localized formation in the trachea or main bronchi, which on thoracic CT may affect more than half of the circumference of the respiratory tract [69]. In these situations, the local tumor expansion caused the tumor to affect the main bronchi, too [70]. In our study, a predominance of SCLC was observed in the upper lobe bronchi (55.55%), while the predominance of ADC was observed in the middle and lower lobe bronchi (66.66%). In literature, the SCLC has been noted to be the second most common LC that occurs in the central bronchi [50]. In most studies, the macroscopic SCLC presents itself as a perihilar localized tumor formation. Large tumors may have extensive necrosis [67]. Only 5%

of SCLC can develop in the peripheral lung parenchyma [71]. From an imaging point of view, the most common pathological aspect in SCLC was the extensive hilar or mediastinal lymphadenopathy secondary to early metastasis [69, 72]. The macroscopic aspects of the bronchoscopically revealed tumors were shown as it follows: superficially infiltrating or invasive lesions (58.33%), the appearance of exophytic or endobronchial mass (22.22%) and mixed lesions (19.44%). Most of the infiltrating lesions were SCC (66.66%), followed by SCLC (23.8%) and ADC (9.52%). The endobronchial masses were ADC (50%), SCC (37.5%), and SCLC type (12.5%). Most of the mixed lesions were ADC (57.14%), SCC (28.57%), and SCLC type (14.28%). The study conducted by Rabahi *et al*. highlighted aspects of endobronchial mass in 64% and mucosal infiltration in 35%, in a group of 199 patients, in whom the most common HP types were SCC in 78 (39%) patients, ADC in 42 (21%) patients, SCLC in 24 (12%) patients and large cell carcinoma in two (1%) patients [73]. In this study, the appearance of endobronchial mass was present in SCC, the mucosal infiltration was the most common finding in the SCLC, while within the ADC the dominant were the luminal narrowing and the external compression (mixed lesions). In other studies, SCLC are tumors that develop peribronchially with infiltration of the bronchial submucosa and the peribronchial tissue [70], and the centrally located bronchial carcinoid visualized with a bronchoscope, had the characteristic bronchoscopic appearance of dark-red, smooth polyposis endobronchial nodules [74]. Partial or important bronchial stenosis has been reported in 22 patients. Half of them (11 patients) had SCC, six (27.27%) patients had ADC and only five (22.72%) had SCLC. Atelectasis was observed in 16 patients. Most atelectasis was reported in SCC in 56.25%, followed by ADC in 31.25%, and SCLC in 12.5% of patients. In our study, the malignant airway obstruction was: endoluminal (intrinsic) in 50% of patients, mixed (combined) in 31.57% and extraluminal (extrinsic) in 18.42% of patients. Most often, SCC have had the appearance of polypoid nodular masses that can cause malignant atelectasis of the central respiratory tract [4]. Endobronchial SCC cause airways obstruction by mass itself leading to pulmonary atelectasis or lobar collapse [49]. Central SCC was the most common HP type of LC causing cavity [72]. The malignant bronchial obstruction has less frequently been observed in patients with SCLC than in those with SCC [4].

Conclusions

LC is still a late-diagnosed condition. FFB remains the most important invasive method of diagnosis of LC of the large airways that enable the precise location of tumors, the assessment of the macroscopic appearance of the tracheobronchial shaft mucosa and tumor lesions, highlighting the degree and obstruction mechanism of the upper respiratory tract. An important advantage is that it also allows the endobronchial biopsy. The most common macroscopic appearance of lung tumors revealed by FFB was the infiltrative appearance. In half of our patients, the malignant bronchial obstruction was achieved by endoluminal mechanism. The most common HP form found in our patients was the SCC, as described in half of the investigated patients.

Conflict of interests

The authors declare that they have no conflict of interests.

Acknowledgments

Viorel Biciuşcă and Mihai Olteanu equally contributed to the manuscript.

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