Article

Not peer-reviewed version

Preoperative Evaluation Management of the Patient with Endobronchial Tumor – Our Experience

Matache Radu Șerban *, Savu Cornel Florentin, Stanciu Gavan Camelia *, Pantile Daniel *, Badescu Camelia, Edan Athir, Iordache Adrian Mihail, Bobocea Andrei Cristian, Vlăsceanu Silviu Gabriel, Mahler Beatrice, Bejgăneanu Andreea Octavia, Nemes Roxana Maria *

Posted Date: 15 August 2023

doi: 10.20944/preprints202308.1070.v1

Keywords: endobronchial tumor; bronchoscopy; tumor board; sleeve resection criteria

Article

Preoperative Evaluation Management of the Patient with Endobronchial Tumor - Our Experience

Radu Serban Matache [1], Cornel Florentin Savu [1], Camelia Stanciu-Gavan [2*], Daniel Pantile [2*], Camelia Badescu [3], Athir Eddan [4], Adrian Mihail Iordache [2], Andrei Cristian Bobocea [1], Silviu Gabriel Vlăsceanu, Beatrice Mahler [5], Andreea Octavia Bejgăneanu [6] and Roxana Maria Nemes [7*]

[1] Department of Thoracic Surgery, "Marius Nasta" Institute of Pneumophtiziology, 050159 Bucharest, Romania;
[2] Department of Thoracic Surgery, "Doctor Carol Davila" Central Military Emergency University Hospital Bucharest, 010825 Bucharest, Romania;
[3] Bronchial Endoscopy Department, "Marius Nasta' Institute of Pneumophtiziology, 050159 Bucharest, Romania;
[4] Tomography Department "Marius Nasta" Institute of Pneumophtiziology, 050159 Bucharest, Romania;
[5] Pneumology Department "Marius Nasta" Institute of Pneumophtiziology, 050159 Bucharest, Romania;
[6] Laboratory Department, Fundeni Clinical Hospital, 022328, Bucharest, Romania;
[7] Pneumology Department "Marius Nasta" Institute of Pneumophtiziology, 050159 Bucharest, Romania; University Titu Maiorescu, Medical School Bucharest,
* Correspondence: camigavan@gmail.com; danielpantile@gmail.com; roxanamarianemes@gmail.com; roxana.nemes@prof.utm.ro

Abstract: Context: Endobronchial tumors are relatively rare. Pathological types are varied, both benign and malignant. Establishing the diagnosis and sleeve resection criteria for such tumors remains a challenge for pulmonologists, bronchoscopists, radiologists, thoracic surgeons, and pathologists. The management of the preoperative assessment of these patients and the establishment of the indication for sleeve resection, represent a big problem. Lung parenchymal sparing surgery remains a challenge, especially in neoplastic patients. **Material and methods**: We carried out a monocentric retrospective study, during the period 2009-2017, on a number of 57 patients. In our center they benefited from clinical examination, radiography, tomography, respiratory function evaluations, autofluorescence bronchoscopy, cardiological evaluation and detection of blood tumor markers. All the patients benefited from the analysis of the tumorboard of our institute and the establishment of the surgical indication for scleev resection. **Results:** Sparing of the lung parenchyma was achieved in case of the 57 patients included in the study. The complex evaluations of laboratory parameters, functional tests, CT examination, bronchoscopy, cardiology, were analyzed by the tumor board, so that the indication for surgical intervention was sleeve resection with preservation of the lung parenchyma. **Conclusions:** We selected patients for sleeve resection, those who presented endobronchial tumors of 2 cm in diameter, with cartilages and bronchial mucosa intact at least 1 cm or 2 cartilages from the formation, on CT and bronchoscopic examination. Cardiological examination and functional tests showed values that do not contradict surgical intervention.

Keywords: endobronchial tumor; bronchoscopy; tumor board; sleeve resection criteria

1. Introduction

Lung cancer is the second most common cancer in men and women in the United States and the leading cause of cancer death in the United States and worldwide [1].

Pure endobronchial neoplasms are a rare entity, and they can present various pathologies [2]. The evaluation of patients with suspected endobronchial lung cancer includes a diagnosis of the primary tumor, an assessment of the extent of spread to regional or distant lymph nodes, or to other structures [3], Preoperative Assessment Prior to Lung Resection [4] and the Thoracic Revised Cardiac Risk Index (ThRCRI) [5]. Lung tumors located centrally, endobronchial, most often have an indication

 doi:10.20944/preprints202308.1070.v1

of massive resection of the lung parenchyma, for which pneumonectomy is frequently performed [4]. Sparing functional lung parenchyma is known to provide a higher quality of life, and sleeve resection have been used as an alternative to pneumonectomy in central lung tumors [5]. In order to perform bronchial resections with bronchoanastomosis, associated or not with lobectomies, a demanding diagnosis is required in terms of localization of endobronchial tumors. In order to establish the surgical indication for resection with sleeve resection, bronchoscopic examination with autofluorescence, tomographic examination, functional explorations and cardiological evaluation are necessary.

Endobronchial tumors usually have symptoms such as cough, hemoptysis, recurrent pneumonia, wheezing, and chest pain [2].

Imaging evaluation by computed tomography scan that highlights the bronchial sign, specifies the characteristics of the target lesion such as size, distance from the hilum and the presence of the bronchus sign [6], bronchi with the cutoff sign [7], tumor analysis according to the Tsuboi classification [8], intratumoral air bronchogram [8].

Flexible bronchoscopy with autofluorescence is necessary for the diagnosis of endobronchial tumor formations. This examination highlights mucosal changes in several degrees of evolution - low-grade (mild and moderate) dysplasias, high-grade (severe and in-situ carcinoma) and invasive carcinoma [9], and evaluates suspicious endobronchial tumors - malignant changes, by detecting irregularities of bronchial mucosa, nodular or polypoid lesions and carina thickening [10].

Establishing the definitive therapeutic attitude of these tumors depends on the location, size and histopathological diagnosis [2].

There is not known a standard protocol for the selection of patients who can undergo endobronchial tumor sleeve resection. We analyzed the literature, NCCN [11] and ESMO [12] Guidelines and established our patient selection criteria.

2. Material and Methods

We performed a monocentric retrospective study, between 2009-2017, to highlight a preoperative selection management of patients with endobronchial tumors who underwent sleeve resection. The present study was carried out after obtaining the Research Ethics Approval number 12707/31.05.2023. In our institute, all the patients upon admission sign a general consent by which they agree to participate in various studies.

Inclusion criteria: Patients who have been diagnosed with endobronchial tumors (located in the primitive and lobar bronchi) detected during computed tomography scan and autofluorescence bronchoscopy; who did not present the situation of locally advanced tumor or secondary determinations; with no severe ventilatory dysfunction; with no severe cardiac dysfunction.

Exclusion criteria: Patients with locally advanced endobronchial tumors, with invasion of neighboring structures, secondary determinations, patients on steroid treatment, functional tests and other comorbidities that contraindicate surgical intervention (severe heart failure, severe respiratory failure); superior vena cava syndrome. Tumors of the trachea, tracheobronchial or located at the level of the hull.

Statistical analysis

Variables were statistically analyzed using Pearson correlations for cardinal variables and Spearman correlations for ordinal variables, respectively. A threshold value of less than 0.05 was considered statistically significant. Statistical calculations were performed using the software application Microsoft Excel (Microsoft 365, Microsoft, USA), respectively Med Calc calculator (MedCalc Software Ltd., 2023).

2.1. The patients

We analyzed the observation sheets of patients who underwent sleeve resection. The following data were collected: sex, age, functional and clinic status, laboratory tests (hemogram, biochemistry

 doi:10.20944/preprints202308.1070.v1

test, tumor markers), size of the lesion, location of the lesion (lobar bronchus, distance from the hilum), appearance on CT, visibility on fluoroscopy (frontal and oblique images) at bronchoscopy, and the anatomopathological diagnostic profile of biopsies. All the patients were analyzed by tumor board.

2.2. Clinical exam

A number of 57 patients, aged between 25 and 75 years, were included in the study. The study group included 11 women and 46 men. Tumors were more frequently located in the right lung: 31 right lung and 25 left lung.

Patients who presented hemoptysis, chest pain, dyspnea, cough, weight loss at admission were included in the study.

2.3. Computer Tomography scan

All the patients underwent native and contrast tomographic examination. Not all the patients were examined in our center. Subjects who presented the bronchus sign on imaging examination, according to the criteria of the TSUBI Classification, were selected. The CT examination had the role of establishing the size of the tumor, the location, the extension and the anatomical relationships that can influence the surgical technique, but also the associated impact on the postoperative evolution of the patient. The endobronchial tumor formation was analyzed - dimensions, regular/irregular outline, homogeneity/non-homogeneity, vascularization, the cutoff sign of the bronchus which specified the degree of its obstruction. The degree of penetrability of the tumor at the level of the bronchial wall was specified. Signs of atelectasis, pneumonitis, pulmonary emphysema were analyzed. Examination of the hilar and mediastinal nodes had an important role. The CT also specified the degree of viability of the lung tissue after bronchial obstruction.

2.4. Bronchoscopy

Bronchoscopic examination was performed under local anesthesia with a flexible bronchoscope with autofluorescence. First, the CT diagnosis was compared with the bronchoscopic diagnosis. At this examination, the lesion was described - location, size, appearance, shape, implantation base, peritumoral mucosa, adjacent necrotic deposits, degree of bronchial obstruction; the degree of bleeding when touched with the bronchoscope; the presence of endobronchial secretions and the collection of biological samples in order to carry out the cytological and bacteriological examination; collection of biopsies to specify the anatomopathological profile. Bronchoscopic examination was performed in the presence of the surgeon, with the exact specification of the number of macroscopically normal cartilages up to the level of the tumor formation.

2.5. Anatomopathological diagnosis

To perform the preoperative anatomopathological diagnosis, biopsy samples were taken during bronchoscopy. They were processed in paraffin. The small amount of tissue taken did not allow the immunohistochemical profile to be performed (Table 1).

Table 1. Characteristics of the studied patients – symptomatology.

	Number of Patients	Percentage (%)
Hemoptysis	54	94,7%
Chest pain	57	100,0%
Dyspnea	49	86,0%
Cough	57	100,0%
Weight loss	46	80,7%

 doi:10.20944/preprints202308.1070.v1

2.6. Functional tests

All the patients underwent ventilatory tests. Only patients with mild and moderate respiratory dysfunction were selected for surgery. Patients who experienced severe respiratory dysfunction were not included in the study.

2.7. Laboratory tests

Laboratory examinations were performed in all patients. Laboratory samples analyzed - hematology, biochemistry, immunology, bacteriology.

2.8. Detection of blood tumor markers

All the patients were tested for tumor biomarkers: squamous cell carcinoma antigen (SCC-Ag), progastrin-releasing peptide (proGRP), chromogranin A (CgA), cytokeratin fragment 19 antigen 21-1 (Cyfra 21-1), carcinoembryonic antigen (CEA) and neuron-specific enolase (NSE).

3. Results

Assessment of the patient's general condition included: age, lung function, cardiovascular status, nutrition and functional status. Characteristics of the studied patients for symptomatology is illustrated in Table 1. Correlations between DLCO values and patients' characteristics. (ASA – American Society of Anesthesiologists, Hb – hemoglobin) is illustrated in Table 2.

Table 2. Correlations between DLCO values and patients' characteristics. (ASA – American Society of Anesthesiologists, Hb – hemoglobin).

	Spearman correlation coefficient	p-value
Age	-0,715	<0,0001
ASA score	-0,548	<0,0001
Height	0,269	0,04
Hb value	-0,148	0,27
Dimensions	0,021	0,88
Hemoptysis	N/A	N/A
Chest Pain	N/A	N/A
Dyspnea	-0,029	0,83
Cough	N/A	N/A
Weight loss	-0,046	0,73

Locoregional evaluation by CT examinationhe followed the sign of the bronchus. Tumor location was type Ia and Ib according to CT-BS classification. Following the evaluation of the patients, the presence of endobronchial tumor formations located at the origin of the right upper lobar bronchus was found in 23 cases, on the upper interlobar spur at the origin of the intermediate bronchus 4 cases, on the right primitive bronchus at the origin of the upper lobar bronchus 2, at the origin of the left upper lobar bronchus 17 cases, at the origin of the left lower lobar bronchus 8 cases and the intermediate bronchus 3 cases. 2 cases of pulmonary emphysema, 4 cases of atelectasis, 4 cases of obstructive pneumonia, 8 cases of bronchiolitis were detected. Characteristics of the studied patients for CT scan is illustrated in Table 3.

Table 3. Characteristics of the studied patients – CT scan.

	Number of Patients	Percentage (%)
Cutoff sign	55	96,5%
Penetrability of the bronchial wall	35	61,4%
Atelectasis	29	50,9%
Mean dimension (cm) [Standard deviation]	1,43 [0,35]	

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 15 August 2023 doi:10.20944/preprints202308.1070.v1

Bronchoscopy with autofluorescence described each formation, which coincided with the specification of computed tomography. The tumor, the appearance of the tumor, its exact location, the degree of obstruction of the bronchus, the mechanism of producing bronchial stenosis and the appearance of the bronchial mucosa were described.

Appearance of endobronchial tumor formations of squamous cell carcinoma – exophytic formation that protrudes into the bronchial lumen, with a wide implantation base, with bronchial infiltration, gray-whitish in color, with black deposits, friable with areas of necrosis. In 13 patients, the peritumoral bronchial mucosa presented a modified appearance. 21 patients had partial bronchial obstruction and 3 had total obstruction. Correlations between the number of free cartilages identified by bronchoscopy and several tumor characteristics is illustrated in Table 4.

Table 4. Correlations between the number of free cartilages identified by bronchoscopy and several tumor characteristics.

	Number	Spearman correlation coefficient	p-value
Laterality		0,098	0,47
Squamos cell carcinoma	24	-0,054	0,69
Adenocarcinoma	13	-0,084	0,53
Typical carcinoid tumor	7	0,187	0,16
Cystic adenoid carcinoma	5	-0,009	0,95
Atypical Carcinoid tumor	4	0,077	0,57
Muco-epidermoid carcinoma	4	-0,064	0,63

The bronchoscopic appearance of endobronchial adenocarcinoma – budded, vegetative infiltrative endobronchial formation, grey-white, with areas of bleeding, infiltrative bronchial mucosa, located at the junction of the bronchi.

Carcinoid - round oval endobronchial lesion, pedicled, well vascularized, brown, located in the middle of the bronchus.

Carcinoma - prominent formation in the bronchial lumen with necrosis, soft, with abundant mucous secretions.

Laboratory analyses - they presented anemia 34 cases, leukocytosis 12 cases, thrombocytosis 3 cases, urea and creatinine slightly increased.

Anatomopathological evaluation detected the following types of tumors: squamous cell carcinoma 24 cases; adenocarcinoma 13 cases; typical carcinoid 7 cases; atypical carcinoid 4 cases; mucoepidermoid carcinoma 4 cases; adenoid cystic carcinoma 5 cases. About 3-6 biopsy fragments were collected by bronchoscopy for each patient. From this tissue was used only for histopathological diagnosis. Immunohistochemistry was not performed. (Correlations between patients' gender and tumor type discovered is illustrated in Table 5).

Table 5. Correlations between patients' gender and tumor type discovered.

Analyzed variable	Number	Spearman correlation coefficient	Value p
squamos cell carcinoma	24	-0.033	0.81
adenocarcinoma	13	0.054	0.69
typical carcinoid	7	0.183	0.17
adenoid cystic carcinoma	5	-0.006	0.97
atypical carcinoid	4	0.134	0.32
mucoepidermoid carcinoma	4	-0.388	0.002

We notice, in the Table 5 that the gender of the patients correlates statistically significant only with one type of cancer, namely muco-epidermoid carcinoma shows an increased affinity for the female gender (r=0.388, p=0.002).

Functional tests - the preoperative evaluation of pulmonary tolerance was done divided into three stages: the first stage consisted of the evaluation of lung function and blood gas analysis, the

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 15 August 2023 doi:10.20944/preprints202308.1070.v1

second stage evaluated the postoperative prediction of lung function, and the third stage was represented by the evaluation of the maximum consumption of oxygen per minute. Selected subjects had postoperative predictive values of forced expiratory volume per second (ppoFEV1) greater than 40%, postoperative predictive diffusing capacity of the lung for carbon monoxide (ppoDLCO) greater than 50%, and peak oxygen. consumption (VO2 max) greater than 15ml/kg/min [13].

Maximum expiratory volume in the first second of a maximal and forced exhalation (FEV_1) is an independent prognostic factor of postoperative risk. Expressing this parameter as a percentage of the predicted value allowed Licker et al. to identify an optimal value of 60% of the predicted as a threshold for moderate-high risk of pulmonary complications [14]

Calculating the predicted postop value (FEV_{1ppo}) is shown in the following formula [15]:

$FEV_{1ppo} = FEV_1$ preop × (1-y)/z

Y=number of functional or unobstructed lung segments that are resected

Z=total number of functional segments (19 - for healthy lungs)

The cardiopulmonary effort test (CPET) is currently considered the "gold standard" for assessing exercise tolerance and estimating pulmonary functional reserve [16,17]. It has the opportunity to globally assess both respiratory and cardiovascular, metabolic and muscular function under conditions of standardized overuse.

VO_{2max} is currently the best predictor of respiratory morbidity [18]: VO_{2max} <10 ml/kg/min (or < 35% of predicted) is a contraindication for pulmonary resection with increased risk of postoperative mortality; VO_{2max} >20 ml/kg/min (or 75% of predicted) allows surgery such as pneumectomy to be performed, defining a low risk class for postoperative complications.

Correlations between age, preoperative FEV1, postoperative FEV1, Hb, sex, are illustrated in the Tables 6 and 7.

Table 6. Characteristics of the studied patients – ventilatory tests, average and STDEV.

	Average	STDEV
Preoperative FEV1 (litres)	4,79	0,74
Preoperative FEV1 (%)	71,58	7,82
Predicted postoperative FEV1 (litres)	3,88	0,67
Preoperative predicted FEV1 (litres)	6,78	1,28
Predicted postoperative FEV1 (%)	57,78	6,77
DLCO	59,79	10,46

Table 7. Characteristics of the studied patients (age, preoperative FEV1, postoperative FEV1, Hb, sex) – ventilatory tests, Spearman correlation coefficient and Value p.

Analyzed variable	Number	Spearman correlation coefficient	Value p
Age		0.639	<0.0001
Preoperative FEV1		-0.172	0.2
Postoperative FEV1		-0.210	0.11
Hb		0.185	0.17
DLCO		-0.548	<0.0001
Sex		-0.019	0.89
Laterality		0.224	0.09

DLCO values do not seem to be influenced by the Hb value, tumor dimensions, symptomatology like hemoptysis, chest pain, dyspnea, cough, or weight loss. However, maybe without any connection with the presence of cancer, DLCO values are influenced by patient's age, ASA score and height. Older patients tend to have lower DLCO values (p=<0,0001), patients with higher ASA score tend to have lower DLCO values (p<0,0001) and taller patients tend to have higher DLCO values (p=0.04).

Cardiological assessment – was performed according to the criteria of the American Heart Association (AHA). The AHA has provided a score to assess the risk of cardiovascular complications in patients undergoing lung resection, the Thoracic Revised Cardiac Risk Index (ThRCRI). All the

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 15 August 2023 doi:10.20944/preprints202308.1070.v1

patients were assessed for cardiac risks based on cerebrovascular and cardiac history, and calculated surgical risks. According to this classification, our patients fell into classes A and B (Table 8).

Blood tumor markers - All the patients were tested for circulating blood tumor markers using ELISA. Patients with squamous cell carcinoma had SCC-Ag present in 19 cases and Cyfra 21-1 16, in those with adenocarcinoma Cyfra 21 - 19 cases, CEA 4 cases; in the case of bronchial carcinoid - chromogranin A (CgA) 9 cases, neuron-specific enolase (NSE) 11 cases and Urinary into 5-hydroxyindoleacetic acid (5-HIAA) 11 cases; carcinoma - Cyfra 21 - 14 cases (Table 8).

Table 8. Correlations between the ASA score and the clinical and paraclinical characteristics of the patients in the studied group.

Analyzed variable	Number	Spearman correlation coefficient	Value p
		antigen	
SCC-Ag	19	0.000	0.99
Cyfra 21-1	29	-0.150	0.26
NSE	11	-0.239	0.07
CEA	4	N/A	N/A
5-HIAA	11	N/A	N/A
CgA	9	-0.516	<0.0001
		Tumor type	
squamos cell carcinoma	24	0.026	0.85
Adenocarcinoma	13	0.013	0.92
Typical carcinoid	7	-0.073	0.59
Adenoid cystic carcinoma	5	-0.078	0.56
Atypical carcinoid	4	-0.014	0.91
Muco-epidermoid carcinoma	4	0.123	0.36

Regarding the correlations between the preanesthetic ASA score and the characteristics of the studied group, we can conclude that a higher ASA score correlates very highly statistically significantly with the age of the patients (Spearman correlation coefficient rho=0.639, p<0.0001), with a value lower DLCO (rho=0.548, p<0.0001) and with the absence of CgA antigen (rho=0.516, p<0.0001). No statistically significant correlations were noticed with the other analyzed characteristics.

Correlations between the discovered tumor type and the analyzed antigens is in Table 9.

Table 9. Correlations between the discovered tumor type and the analyzed antigens.

Analyzed variable	Number	Spearman correlation coefficient	Value p
squamos cell carcinoma		24	
Laterality		-0.106	0.43
SCC-Ag	19	0.829	<0.0001
Cyfra 21-1	16	-0.019	0.89
NSE	0	N/A	N/A
CEA	0	N/A	N/A
5-HIAA	0	N/A	N/A
CgA	0	N/A	N/A
Adenocarcinoma		13	
Laterality	9	0.143	0.29
SCC-Ag	0	-0.384	0.003
Cyfra 21-1	9	0.025	0.85
NSE	0	-0.426	0.0009
CEA	4	N/A	N/A
5-HIAA	0	N/A	N/A
CgA	0	N/A	N/A
Typical carcinoid		7	

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 15 August 2023 doi:10.20944/preprints202308.1070.v1

Laterality		-0.100	0.46
SCC-Ag	0	-0.265	0.05
Cyfra 21-1	0	N/A	N/A
NSE	7	0.426	0.006
CEA	0	N/A	N/A
5-HIAA	7	N/A	N/A
CgA	6	-0.356	0.01
Adenoid cystic carcinoma		5	
Laterality		0.149	0.27
SCC-Ag	0	-0.219	0.10
Cyfra 21-1	3	-0.082	0.54
NSE	0	N/A	N/A
CEA	0	N/A	N/A
5-HIAA	0	N/A	N/A
CgA	0	N/A	N/A
Atypical carcinoid		4	
Laterality		-0.172	0.20
SCC-Ag	0	-0.194	0.15
Cyfra 21-1	0	N/A	N/A
NSE	4	N/A	N/A
CEA	0	N/A	N/A
5-HIAA	4	N/A	N/A
CgA	3	0.356	0.01
Muco-epidermoid carcinoma		4	
Laterality		0.104	0.44
SCC-Ag	0	-0.194	0.15
Cyfra 21-1	1	0.052	0.70
NSE	0	N/A	N/A
CEA	0	N/A	N/A
5-HIAA	0	N/A	N/A
CgA	0	N/A	N/A

We notice in the table above that, in epidermoid carcinoma, the SCC-Ag antigen is present with a very high statistical significance (Pearson correlation coefficient r=0.829, p<0.001), the other antigens do not show a specific affinity towards this tumor type. In the case of adenocarcinomas, we observe a correlation of tumor type with the absence of SCC-Ag antigens (r=0.384, p=0.003) and CEA (r=0.426, p=0.0009). We also note that in the case of typical carcinoids there is also the absence of SCC-Ag (r=0.265, p=0.05), but CEA is present (r=0.426, p=0.006). In the case of atypical carcinoid, we notice a statistically significant correlation with the presence of CgA antigen (r=0.356, p=0.01). No other statistically significant correlations were observed between the type of cancer and the presence of certain antigens.

STAGING - The tumors studied were in stage II - 21 cases and in stage III - 36 cases.

Frank C. Detterbeck in "The eighth edition TNM stage classification for lung cancer", stage II involves either T2b/T3 N0 M0 tumors or T1/T2 N1 M0 tumors. Stage III is now divided into three subgroups. Stage IIIA includes T4 N0 M0 and T3/4 N1 M0 tumors as well as T1/T2 N2 M0 tumors [19].

The tumor board of our center that analyzed these cases was made up of: pneumonologist, radiologist, bronchoscopist, cardiologist, thoracic surgeon, anatomopathologist, oncologist, radiotherapist.

The imaging data of endobronchial tumor resectability with a maximum diameter of 2 cm, two intact bronchial cartilages above and below the pathological area; which does not exceed the anatomical structure of the bronchus, were analyzed; autofluorescence bronchoscopy – highlighted

 doi:10.20944/preprints202308.1070.v1

as elements of resectability at least 2 upper and lower bronchial cartilages of tumor without aspects of tumor infiltration, the associated pathologies, functional tests, the histological type of the tumor.

4. Discussions

Lung parenchymal sparing surgery remains a clinical challenge. In this study, we performed a single-center retrospective study of patients who underwent resection with sleeve resection for endobronchial tumors. The purpose of the study was to inform our selection criteria of patients who can undergo resection with sleeve resection. A number of 57 subjects with endobronchial tumors were analyzed in terms of CT examination, autofluorescence bronchoscopy, functional tests, cardiological examination, laboratory examination, detection of serological tumor markers.

The CT examination revealed the presence of the bronchus sign and bronchial cutoff [6–8]. All tumor formations were prominent in the lumen of the bronchus and were visualized on native and contrast-enhanced CT.

Bronchoscopic examination with autofluorescence confirmed the presence of endobronchial tumor formations and specified the appearance of the tumor, its exact location, the degree of obstruction of the bronchus, the mechanism of producing bronchial stenosis and the appearance of the bronchial mucosa. [9,10]. It is known that the role of autofluorescence bronchoscopy is to detect malignant and premalignant lesions of the bronchial mucosa [20]. This type of bronchoscopic examination highlights the existence of a malignant infiltration in the bronchial mucosa and allows us to assess how much cartilage is intact from the level of the endobronchial tumor and to assess the possibility of performing a resection with sleeve resection.

Taking biopsies from these formations establishes the anatomopathological diagnosis, but not always enough tissue is taken to process the immunohistochemical profile.

Serological analysis of serological tumor markers is known in current practice. Specialized studies have highlighted their detection through various other determinations (biochemical, electrochemical on sensors) [21–23]. The correlation between the CT image, bronchoscopy and the presence of blood tumor markers Cifra-21, NSE, CEA, SCC-Ag, chromogranin A (CgA), 5-hydroxyindoleacetic acid (5-HIAA) is known in the literature [7,24–27].

The evaluation of the functional tests of the studied patients revealed moderate and mild ventilatory dysfunctions. The following were studied: preoperative FEV1 (LITERS); Postoperative FEV1 (liters); FEV 1 preoperative liters; Postoperative FEV1 % according to the Algorithm for assessing cardiovascular status before lung resection, the evaluation of hemodynamic parameters and postoperative risks [5,28–31].

Limitations of the present study - monocentric study, small number of cases.

5. Conclusions

The indications for the sleeve resection of endobronchial tumors and implicitly the preservation of the lung parenchyma, remain a great challenge. The selection criteria are not well known. We consider our management of the preoperative assessment – a beginning of extensive research and development of a guideline regarding the selection criteria for sleeve resection.

Author Contributions: Conceptualization, R.S.M. and C.S.G.; Data curation, A.M.I., C.F.S. and B.M.; Formal analysis, P.D. and A.O.B.; Investigation, C.S.G., P.D. and A.E.; Methodology, R.M.N., C.S.G. AND R.S.M.; Project administration, R.S.M..; Resources, A.C.B., B.C. E.A. and D.G.V.; Software, P.D.; Supervision, R.M.N. and R.S.M.; Visualization, R.M.N; Writing—original draft, C.S.G. and A.O.B.; Writing—review and editing, R.S.M., C.S.G., R.M.N. and A.O.B. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: The present study was carried out after obtaining the Research Ethics Approval number 12707/31.05.2023, "Marius Nasta" Institute of Pneumonology, 050159 Bucharest, Rumania.

Informed Consent Statement: In "Marius Nasta" Institute, all the patients upon admission sign a general consent by which they agree to participate in various studies.

Data Availability Statement: The data underlying this article will be shared on reasonable request to the corresponding author.

Acknowledgments: We thank the "Marius Nasta" Institute for the support and help provided.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Kim, J.; Lee, H.; Huang, B.W.; Lung Cancer: Diagnosis, Treatment Principles, and Screening. Am Fam Physician 2022, 105, 487-494.
2. Pandey, K.; Vaidya, P.J.; Kate, A.H.; Chavhan, V.B.; Jaybhaye, P.; Patole,K.; Deshpande,R.K.; Chhajed, P.N.; Bronchoscopic and Surgical Management of Rare Endobronchial Tumors - Brief Communication. J Can Res Ther 2016, 12,1093-1097, DOI: 10.4103/0973-1482.186692
3. Magouliotis, D.E.; Zotos, P-A.; Karamolegkou, A.P.; Tatsios, E.; Spiliopoulos, K.; Athanasiou, T.; Long-Term Survival after Extended Sleeve Lobectomy (ESL) for Central Non-Small Cell Lung Cancer (NSCLC): A Meta-Analysis with Reconstructed Time-to-Event Data. J. Clin. Med. 2023,12, 204, https://doi.org/10.3390/jcm12010204
4. Thomas, D.C.; Blasberg, J.D.; Arnold, B.N.; Rosen, J.E.; Salazar, M.C.; Detterbeck, F.C.; J. Boffa, D.J.; Anthony W. Kim, A.W.; Validating the Thoracic Revised Cardiac Risk Index Following Lung Resection. Ann Thorac Surg; Predicting Cardiac Complications 2017,104,389–394, http://dx.doi.org/10.1016/j.athoracsur.2017.02.006
5. Megawati, D.; Rasmin, M.; Antariksa, B.; Yunus, F.; Preoperative Assessment Prior to Lung Resection: How to Eliminate the Risk. Breath Sci. 2022; 2(3): 175-185 https://doi.org/10.36497/respirsci.v2i3.48
6. Bilaçeroğlu, S.; Kumcuoğlu, Z.; Alper, H.; Osma, E.; Çağırıcı, U.; Gunel, Ö.; Bayol, Ü.; Celikten, E.; Perim, E.; Timur Köse, T.; CT Bronchus Sign-Guided Bronchoscopic Multiple Diagnostic Procedures in Carcinomatous Solitary Pulmonary Nodules and Masses. respiration 1998,65 (1), 49–55; https://doi.org/10.1159/000029237
7. Zhang, X.; Lv, F.; Fu,B.; Li,W.; Lin, R.; Chu, Z.; Clinical and Computed Tomography Characteristics for Early Diagnosis of Peripheral Small-cell Lung Cancer. Cancer Management and Research 2022, 14, 589-601. https://doi.org/10.2147/CMAR.S351561
8. Imabayashi, T.; Matsumoto, Y.; Uchimura, K.; Furuse, H.; Tsuchida, T.; Computed Tomography Bronchus Sign Subclassification during Radial Endobronchial Ultrasound-Guided Transbronchial Biopsy: A Retrospective Analysis. Diagnostics 2023, 13, 1064. https://doi.org/10.3390/diagnostics13061064
9. Badescu, C.; Mihălțan, F.; Autofluorescence Bronchoscopy and Lung Cancer Diagnosis. Pulmonology, vol 69, 2020, 135-141, DOI: https://doi.org/10.2478/pneum-2021-0002
10. Liu, Z.; Zhang, Y.; Li, Y-P.; Ma, J.; Shi, F.; Zhao, D-F.; Li, J-M.; Zhang, Y-Z.; Clinical Relevance of Using Autofluorescence Bronchoscopy and White Light Bronchoscopy in Different Types of Airway Lesions. Journal of Cancer Research and Therapeutics - 2016, 12, 69-72. DOI: 10.4103/0973-1482.147731
11. NCCN Clinical Practice Guidelines in Oncology, Non-Small Cell Lung Cancer, Version 3, 2020. https://www2.tri-kobe.org/nccn/guideline/lung/english/non_small.pdf
12. Remon, J.; Soria, J-C.; Peters, S.; Early and Locally Advanced non-small-cell Lung Cancer: an update of the ESMO Clinical Practice Guidelines focusing on Diagnosis, Staging, Systemic and Local Therapy. Ann Oncol. 2021, 32(12), 1637-1642. two: 10.1016/j.annonc.2021.08.1994.
13. Spyratos, D.; Zarogoulidis, P.; and all; Preoperative evaluation for lung cancer resection - Review article. J Thorac Dis 2014, 6, S162-S166. doi: 10.3978/j.issn.2072-1439.2014.03.06
14. Licker, M.J.; Widikker, I.; Robert, J.; Frey, J.G.; Spiliopoulus, A.; Ellenberger, C.; and all; Operative mortality and respiratory complications after lung resection for cancer: impact of chronic obstructive pulmonary disease and time trends. Ann Thorac Surg 2006, 81, 1830-1837.
15. Roy, P.M.; Preoperative pulmonary evaluation for lung resection. J Anaesthesiol Clin Pharmacol 2018, 34, 296-300. doi: 10.4103/joacp.JOACP_89_17. PMID: 30386009; PMCID: PMC6194844.
16. American Thoracic Society, American College of Chest Physicians. ATS/ACCP statement on cardiopulmonary exercise testing. American Journal of Respiratory and Critical Care Medicine 2003, 167,211–277.
17. Wasserman, K.; Hansen, J.E.; Sue, D.Y.; Stringer, W.W.; Sietsema, K.E.; Sun, X.G.; and all; Principles of exercise testing and interpretation. 5th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2012.

18. Bechard, D.; Wetstein, L.; Assessment of exercise oxygen consumption as preoperative criterion for lung resection. The Annals of Thoracic Surgery 1987, 44, 344–349.
19. Detterbeck, F.; and all; The Eighth Edition Lung Cancer Stage Classification. CHEST 2017, 151, 193-203.
20. Zaric, B.; Stojsic, V.; Sarcev, T.; Stojanovic, G.; Carapic, V.; Perin, B.; Zarogoulidis, P.; and all; Advanced Bronchoscopic Techniques in Diagnosis and Staging of Lung Cancer. J Thorac Dis 2013, 5, S359-S370. doi: 10.3978/j.issn.2072-1439.2013.05.15
21. Nistor, C.E.; Stanciu-Găvan C.; Clinical Implications of Early Molecular Diagnosis in Lung Cancer - brief review. J Addict Med Ther Sci 6(1), 2020, 026-029. TWO:https://dx.doi.org/10.17352/2455-3484.000033
22. Nistor C.E.; Stefan-van Staden, R.I.; Dumitru, A.V.; Stanciu Gavan, C.; A Screening Test for Early Diagnosis of Microcellular Bronchopulmonary Cancer-Pilot Study. J. Clin. Med. 2020, 9, 76. doi:10.3390/jcm9010076
23. Comnea-Stancu, I.R.; Stefan-van Staden, R.I.; van Staden, J.F.; Stanciu-Gavan, C.; Stochastic Sensors based on Maltodextrins for Screening of Whole Blood for Neuron Specific Enolase, Carcinoembryonic Antigen and Epidermal Growth Factor Receptor. Microsyst Technol 2016, 22, 25–29. DOI 10.1007/s00542-015-2635-z
24. Li, Y.; Tian, X.; Gao, L.; Jiang, X.; Fu, R.; Zhang, T.; Ren, T.; Hu, P.; Wu, Y.; Zhao, P.; Yang, D.; The Location, Histological Type, and Stage of Lung Cancer are associated with Bleeding during Endobronchial Biopsy. Cancer Management and Research 2018, 10, 1251–1257. http://dx.doi.org/10.2147/CMAR.S164315
25. Herath, S.; Rad, H.S.; Radfar, P.; Ladwa, R.; Warkiani, M.; O'Byrne, K.; Kulasinghe, A.; The Role of Circulating Biomarkers in Lung Cancer. Frontiers in Oncology 2022, 11, 1-13. two: 10.3389/func.2021.801269
26. Liu, L.; Teng, L.; Zhang, L.; Cong, P.; Yao, Y.; Sun, G.; Liu, Z.; Yu, T.; Liu,M.; The Combination of the Tumor Markers Suggests the Histological Diagnosis of Lung Cancer. Hindawi BioMed Research International 2017, 1-9. https://doi.org/10.1155/2017/2013989
27. Guo, S.; Chen, J.; Hu, P.; Li, C.; Wang, X.; Chen, N.; Sun, J.; Wang, Y.; Wang, J.; Gu, W.; Wu, S.; The Value of Circulating Tumor Cells and Tumor Markers Detection in Lung Cancer Diagnosis. Technology in Cancer Research & Treatment 2023, 22, 1-11. DOI: 10.1177/15330338231166754
28. Brunelli, A.; Kim, A.W.; Berger, K.I.; Addrizzo-Harris, D.J.; Physiological Evaluation of the Patient with lLng Cancer being considered for Resectional Surgery: Diagnosis and Management of Lung Cancer, 3rd. American College of chest physicians evidence-based clinical practice guidelines. Thing. 2013, 143, 166-190.
29. Burke, J.R.; Duarte, I.G.; Thourani, V.H.; Miller, J.I.; Preoperative Risk Assessment for Marginal patients Requiring Pulmonary Resection. Ann Thorac Surg. 2003, 76, 1767-1773.
30. Motono, N.; Ishikawa, M.; Iwai, S.; Iijima, Y.; Usuda, K.; Uramoto, H.; Individualization of Risk Factors for Postoperative Complication after Lung Cancer Surgery: a Retrospective Study. BMC Surg. 2021, 21, 1-8.
31. Saleem, A.; Syed, W.; Bhat, A., et al.; Changes in Blood Gases and Hemodynamic Parameters in Patients undergoing Lung Resection Surgery and its Clinical Implications. J Cardiothorac Med. 2019, 77(1), 7, 406-412.