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Accuracy and efficacy of imagig guided lung biopsies in the therapeutic management of tumors with pulmonary localization

SUMMARY OF THE THESIS

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Contained

LIST OF PUBLISHED SCIENTIFIC PAPERS

ARTICLES: mention is made of the title of the journal, volume, year, number, as well as the impact factor, with links to the respective publications

1. **Betianu CI**, Ion G, Goicea M. Mimickers of Lung Cancer: When Not to Perform a Pulmonary Biopsy - Case Reports. Intern Med. 2019;16(5):59–68. Impact Factor: 0.36 (JCR 2020)
   http://dx.doi.org/10.2478/inmed-2019-0085
2. **Bețianu CI**, Goicea M, Ion G, Bondari A. Is transthoracic lung biopsy a safe procedure? Med Ultrason. 2020;22(1):114–5. Impact Factor: 1.6 (JCR 2020)
   http://dx.doi.org/10.11152/mu-2362
3. **Betianu CI**, Neagu A V., Pantile D, Pascariu AD, Bajenaru A, Neagu AI, et al. Percutaneous lung biopsy: Should it be avoided or not? Arch Balk Med Union. 2020;55(4):616–23. Impact Factor: 0.13 (SJR 2021)
   http://dx.doi.org/10.31688/ABMU.2020.55.4.08

ORAL PRESENTATIONS, CONFERENCES AND CONGRESSES:

1. Goicea M, **Betianu CI**. Picking the lesion to pick on: Comparing diagnostic accuracy and complications rate in patients with lung versus non-lung imaging-guided biopsies. In ECR 2019; 2019.
2. Ion G, **Betianu CI**. Lung ultrasound in dyspneic patients. In ECR 2019; 2019. Available from: https://dx.doi.org/10.26044/ecr2019/C-1383

LIST OF ABBREVIATIONS

ADK - Adenocarcinoma

CT – Computer Tomography

FNA – Fine needle aspiration

Ga - Gauge

INR - International normalized ratio

NST - No Specific Type

PET-CT - Positron emission tomography

Introduction

Primitive lung carcinoma has a high incidence and mortality and continues to represent one of the major health problems globally. According to Globocan 2020, lung neoplasm is the main type of cancer, with an incidence of 2206771 (11.4% of all cancer cases), approximately equal to the incidence of breast cancer but with a much higher mortality rate of 18% compared to 6.9% of total deaths from cancer. [1] In Romania, 12122 newly diagnosed cases of lung cancer were reported in 2020 (12.3%). The mortality rate of 10779 deaths recorded in the same year is by far the highest, with a percentage of 19.8%.

For the oncologist to make a good treatment plan, he or she needs to know a lot about both the histopathological type and the genetic profile.

The concept of percutaneous imaging-guided biopsy is becoming increasingly popular, and we can say that it underlies the histopathological diagnosis of tumors regardless of their location. It is routinely used in our hospital, and we believe it is a safe procedure with limited morbidity and very low mortality.

The term "biopsy" refers to both trucut-needle biopsy and fine-needle aspiration biopsy, often known as "FNA". Trucut biopsy provides fragments for histopathological study, while FNA provides aspirates for cytological analysis.

Although it is a basic technique in the arsenal of interventional medicine, well studied and consolidated, it is not possible to accurately specify its place in the tumor diagnostic algorithm. The indications for biopsy evolve continuously, but it is certain that percutaneous biopsy is one of the pillars that support the patient's rapid path to a treatment line. But there is a lack of agreement on the best way to biopsy patients with lung nodules and beyond. This situation is a direct result of the lack of evidence in this area, as seen by the dramatic variation in the rates of complications reported in the literature. [2]

As an increasing number of people present newly discovered lung nodules following lung cancer screening programs, more and more discussions are emerging about whether or not to biopsy the nodules. These dilemmas will undoubtedly become more widespread. This technique may not be appropriate for some patients, such as those with a low likelihood of having malignant nodules, those who are too exhausted to undergo

radiotherapy or chemotherapy, or those who have a high risk of developing cancer and should be treated surgically.[3,4]

So, before exposing patients to the morbidities associated with an imaging-guided biopsy, doctors need to make sure that patients fully understand the dangers involved. Although it can be performed technically on almost any organ, that does not mean that it is the most appropriate management option for the patient. It is still in debate whether choosing surgical treatment as the first step in diagnosing a lung tumor is the right option. [5] Several authors say that the costs and risks of percutaneous biopsies can be avoided when the imaging is typical of malignancy or benignity. They also say that tumors can be removed effectively without increasing morbidity or cost when a percutaneous biopsy is done at the same time.

To sum up, this is a complicated subject, but the main goal should be to find the diagnostic procedure that fits the patient's situation best.

1. Review of Literature:

1.1. Indications and contraindications of lung biopsy

1.1.1. Indications of percutaneous lung biopsy

The purpose of the lung biopsy is to specify the etiology of a nodule or lung mass, that is, to determine the nature of the collected material. In the case of nodules with a malignant suspicion, the biopsy is useful for specifying the histopathological type, which is essential in the planning of oncological treatment.[6] Even within a histological subtype of cancer, there is significant variability in cancer behavior and response to therapy. The identification of an oncogene, followed by the administration of a targeted specific inhibitor, is the basis of personalized cancer treatment.

There are multiple indications for performing lung biopsy. Below we will mention those stipulated in the British Thoracic Society[5]:

- Newly emerged lung nodule or growing lung nodule that cannot be approached by bronchoscopic biopsy;
- Multiple lung nodules in a clinically healthy patient or without a known neoplasm;
- Persistent lung infection that could not be successfully investigated by sputum analysis, serology or bronchoscopy;

- Hilar mass that can not be bronchioscopically evaluated or at which the bronchoscopic result is negative.

NCCN (National Comprehensive Cancer Network) and ACCP (American College of Chest Physicians) recommendations are more elaborate and include several clinical scenarios. [7] What they have in common is the recommendation to make the histopathological diagnosis by the least invasive method when the substrate of the lesion is a questionable one.

1.1.2. Contraindications of percutaneous lung biopsy

The decision and planning of a lung biopsy should be discussed in a multidisciplinary committee to balance the benefits and risks of this procedure. The members of this committee vary depending on the type of pathology or organ approached. At the same time, the pulmonary biopsy cannot be performed without the patient's informed consent. If the patient does not agree with the procedure, then he will be given another alternative method of diagnosis. Being a minimally invasive procedure, there are a number of relative contraindications to lung biopsy. These are[8]:

- Hemorrhagic diathesis;
- Respiratory failure, mechanical ventilation, pneumectomy, pulmonary hypertension;
- Pulmonary pseudolesions such as arteriovenous malformations, hydatid cyst, inflammations, etc.;
- Uncooperative patient.

1.2. Complications of biopsy and their management

Transthoracic pulmonary biopsy is considered a relatively safe minimally invasive procedure. But it is among the procedures with the highest rate of complications performed by radiologists. Among them are: pneumothorax, alveolar hemorrhage, subcutaneous local hematoma. [9] Other complications such as hemotorax, air embolism, hemomediastinum, cardiac tamponade, vasovagal reaction, or tumor seeding are reported very rarely, due to rigorous preparation.

There are studies that indicate an overall complication rate after transthoracic biopsy of up to 45%, but severe complications that require further further interventions such as, for example, the installation of a pleurostomy or blood transfusion, are reported in less than 6% of cases. [10] Complications of transthoracic lung biopsy can be classified into:

- Non-vascular complications: pneumothorax, gaseous embolism, tumor sowing, infection;
- Vascular complications: alveolar hemorrhage, hemotorax, subcutaneous hematoma.

The radiologist who performs the pulmonary biopsy should be familiar with the possibility of possible complications, to recognize and treat them as much as possible or to transfer the patient to the other wards: thoracic surgery, general surgery, urgent, ICU. In any interventional radiology room there must be a resuscitation kit and a pleural drainage tube. In case of symptomatic complications, it is necessary first of all to interrupt the transthoracic biopsy and monitor vital functions: oxygen saturation, blood pressure and pulse. The specific treatment is approached for each complication separately in the following.

2. Personal contributions

2.1. Working hypothesis and general objectives

In interventional radiology, percutaneous biopsy is a widespread technique, well known and very well studied. From the experience gained through the interaction with the other medical and surgical specialties, we have noticed some reluctance related to both the necessity and usefulness of the procedure and an overestimation related to the possible associated complications.

A procedure is truly justified if it has the potential to influence the diagnosis and management of treatment. We need to balance this concept with the level of risk of the procedure, because, including a minimally invasive procedure, it has associated risks that need to be assessed. In addition to the rate of complications, accuracy is another decision factor in the choice of the diagnostic procedure.

Imaging guidance is very important in performing interventional procedures, especially when there are structures with high potential for complications, adjacent to the lesions of interest. Understanding the choice of the organ to be biopsied and the puncture technique has as main purpose, the improvement of the diagnosis, the prognosis and the possibility of performing a larger number of tests in order to establish personalized treatments depending on the primary tumor location.

Thus, it is important in this study to stipulate the imaging methods of guidance and to compare them in order to decrease the rate of complications and increase the accuracy of the diagnosis in order to improve survival and quality of life and initiate targeted therapeutic strategies.

In order to specify with more certainty the role of percutaneous biopsy in the diagnosis and staging of cancers, and to get acquainted with it, it is necessary to know the safety profile of the procedure and whether the rate of complications is low enough to replace the biopsy of the surgical type. Through this accumulated knowledge we will reduce the chances of subjecting patients to dangerous interventions.

In addition to those mentioned, this study aims to decrease the number of unnecessary biopsies and pulmonary interventions, on lesions that do not require a certain histopathological diagnosis or treatment because they have minimal chances of being malignant or of endangering the patient's life. This will be achieved by listing, describing and presenting the lesions that mimic lung cancer, also called pseudolesions. These lesions have typical imaging appearance and do not require puncture for diagnostic purposes.

Another issue addressed in this study, which I consider to be very important, is the patient with multiple injuries. The lung is a common place for both primitive and secondary tumors, so patients with oncological lung lesions have a high chance of having oncological lesions in other organs as well. Whether the patient presents himself for diagnosis, staging or changing the oncological treatment line, the radiologist takes into account for biopsy the lesions with oncological suspicious appearance, new or evolving lesions, the patient's morbidity and the oncologist's indications. The study comparatively analyzes the complication rate for lung biopsies and biopsies in other organs to answer the question of whether avoiding lung biopsy in favor of another organ is the right and safe decision for the patient.

2.2. General methodology of the research

The protocol of the study was approved by the Ethics Commission of the Central Military Emergency University Hospital "Dr. Carol Davila" in Bucharest, Romania.

All participants in the studies carried out in our clinic expressed their consent and signed the informed consent. All patient data tracked in this study respects the confidentiality nature.

We collected the data in collaboration with the team of the Radiology and Medical Imaging Clinic within the Central Military Emergency University Hospital "Dr. Carol Davila".

For this study, a systematized sampling plan of patients was not implemented, who were recommended for biopsy punctures by oncologists, surgeons and other specialties.

The study has the following design:

- Clinical study evaluating the observation sheets from which personal data, clinical and laboratory aspects were recorded
- Imaging study
- Statistical study
- Study of the specialized literature according to the new guidelines both for the elaboration of the general part and for the capitalization of the special part
- Elaboration within the study of 3 articles and another 2 posters at International Congresses
- Two separate batches of patients were included in the study, thus achieving two substudies
    - A main batch of 558 biopsies on 535 patients, of wich:
        - 355 lung biopsies
        - 203 biopsies from other organs
    - A separate group of 52 pulmonary biopsies with statistical analysis of histopathological results
- Exclusion criteria:
    - Refusal of 45 patients
    - Deteriorated clinical condition
    - Modified laboratory analysis

The history and evolution of the patients were thoroughly evaluated and we recorded demographic data (age and sex), clinical information (INR (international normalised ratio), blood glucose levels, smoking status, body mass index, the presence of diabetes mellitus, blood pressure values, personal pathological history, heredocolateral history) and information on how to carry out the procedure (if the procedure has been repeated before,

biopsy organ, type of procedure, imaging guidance, needle size in gauge, complications, interventions, histopathological result, maximum tumor size, number of fragments obtained) for conducting the study.

We considered as minor complications those that did not require intervention and major complications those that required intervention.

The statistical study was conducted using IBM SPSS Statistics (Version 20) and Microsoft Excel (Version 2019).

Patients sent to our clinic by oncologists, surgeons or other specialties were consulted by a primary radiologist (C.I.B.) who performed preprocedural planning. The patient already had CT, MRI or PET-CT imaging examinations performed recently, otherwise they were performed in our clinic.

2.3. Study of the safety profile of percutaneous lung biopsy

Transthoracic lung biopsy is a minimally invasive diagnostic procedure used, for the most part, to determine the management of patients with high suspicion for malignant lung damage. Despite the fact that several [2,20,21] have elucidated the basic role of percutaneous pulmonary biopsies, we have noticed that both patients and doctors consider percutaneous pulmonary biopsies dangerous, especially in light of the potential for complications.

In our hospital, between July 2015 and June 2018, percutaneous pulmonary biopsies of the "core biopsy" type were performed on a group of 317 patients. The procedures were performed under either CT guidance or ultrasound guidance, and trucut needles with a diameter of 18 Gauge were used.

Based on CT scans, the biopsy indication and the choice of puncture site were determined; this was also considered appropriate for subsequent ultrasound-guided procedures, since the morphological correlation between CT and ultrasound in lung damage is reliable. [22]

Complications occurred in 33 cases (10.41%) of the 317 patients: 25 pneumothorax (7.89%), 3 hemotorax (0.95%), 7 local alveolar hemorrhages (2.21%) and 1 infection at the puncture site (0.32%) in a patient with decompensated diabetes mellitus. There were no cases of gaseous embolism, sowing on the needle path and no deaths.

In conclusion, percutaneous pulmonary biopsies are a generally safe diagnostic treatment, provided that the patients are properly selected. Complication rates in our hospital are similar to statistics from larger global research.

2.4. Study of lesions mimicking lung cancer

2.4.1. Introduction

There is a wide range of pulmonary pseudolesions that can mimic both the imaging aspect of pulmonary neoplasia and their clinical manifestations. The pulmonary pseudolesions described in the literature are round atelectasis, round pneumonia, hamartoma, sclerosing hemangioma, tuberculoma, inflammatory pseudotumor, etc.

2.4.2. Materials and methods

This study presents a series of patients with focal lung lesions hospitalized between 2016 and 2018 in the "Carol Davila" Central Military Emergency University Hospital, Bucharest, Romania. The six cases presented were sent to the Department of Radiology for percutaneous imaging-guided lung biopsy being suspected of malignant lesions. Each case was carefully analyzed by reassessing the thoracic CT imaging examinations in conjunction with clinical and paraclinical information from the patient record.

2.4.3. Results and Discussions

Many lung lesions involving the parenchyma, pleura or vascular structures tend to mimic malignant lung lesions. In this paper, we evaluate six pulmonary pseudolesions encountered in our clinic that were initially mistaken for a pulmonary neoplasm.

Round pneumonia

Round pneumonia refers to any pneumonia that presents itself as a nodule or "coin lesion" of the lung. Round pneumonia is considered a pediatric disease; in adults, it is a rare disease, accounting for less than 1% of the "coin lesions" of the lung.

The imaging aspect reveals a round lung lesion with slightly diffused edges, most often localized in the posterior segments or lower lobes. At CT scan, round pneumonia occurs as a mass of heterogeneous structure with tissue-type attenuation, with small satellite lesions and associated pleural thickening.

Pulmonary infarction

Pulmonary infarction is a frequent complication of pulmonary embolism, which develops in about 15% of patients with pulmonary thromboembolism. Consolidation from pulmonary infarction is due to alveolar blood flooding, which associates inflammatory reaction around central necrosis. Pulmonary thromboembolism produces more pressure in the pulmonary circulation. Alveolar hemorrhage is the result of increased vascular permeability and damage to the capillary endothelium triggered by pulmonary hypertension.

On CT examination, pulmonary infarction occurs as a peripheral, juxtapleural, triangular-shaped consolidation, with the base towards the periphery (Hampton hump), with inhomogeneous structure by the presence of aerated, non-crystalphilic bubble areas and without an air bronchogram. The presence of aerated bubbles in the center of a peripheral consolidation has a specificity of 98% and a sensitivity of 46% for pulmonary infarction[23]. The sign of the feeding vessel, which refers to an enlarged vessel that goes to the tip of the infarction area, can also be associated. Sometimes the lesion can cavita, in cases of septic embolism or superinfection of a thrombembolism.

Round atelectasis

Round atelectasis is a type of atelectasis of the lung associated with thickening of the adjacent pleural leaf that can mimic a malignant lung injury. It is found in the literature under several names such as folded pulmonary syndrome or Blesovsky syndrome, pleuroma, pleuritis with atelectasis, helical or cylindrical atelectasis.

For the differentiation of round atelectasis from a malignant pulmonary mass we help ourselves by several visible ct imaging features. First of all, round atelectasis has associated interstitial bands in the "comet tail", which is a specific sign of this lesion and can be observed almost in all cases. The sign of the comet tail is given by the bronchi and vessels entering the lesion. Another sign associated with round atelectasis is "raven's claw" (Crow's feet), dense interstitial bands that irradiate from the round mass into the lung parenchyma.

Pseudoaneurymism of pulmonary artery

Pseudoaneurymism of the pulmonary artery is a focal dilation of the artery involving only the two external layers of the arterial wall: the media and adventition. Pseudoaneurymism of the pulmonary artery is a rare diagnosis but with potentially fatal

complications. It can be congenital or acquired; the most common causes of acquired pulmonary pseudoaneurym are infectious diseases, chest wall trauma or trauma caused by pulmonary catheters.

In pseudoaneurysm of the pulmonary artery, CT examination with contrast substance is "gold standard" and reveals a fusiform or sacciform filling addition that presents continuity solution with an adjacent vessel, which can sometimes be partially thrombosed. A key feature of the lesion is that it has iodophilia similar to that of the pulmonary artery in all phases of the examination. Other signs may also be present, such as thickened arterial walls that indicate vasculitis, tensile bronchiectasis, tuberculosis or a pyogenic infection. [24] They are usually solitary lesions, except in cases where they are caused by endocarditis or a metastatic disease.

Pulmonary seizure

Pulmonary seizure is a congenital pulmonary anomaly characterized by a non-functional region of the lung that is not connected to the normal tracheobronchical tree and has systemic arterial intake. This pathology should be suspected in any patient with recurrent pneumonia in the lower lobe. There are two types of pulmonary seizure: intralobar (most commonly) and extralobar. Intralobar seizure has no separate pleural leaf and has venous drainage through the pulmonary veins in most cases. Extralobar seizure has a separate pleural leaf, and venous drainage is done through systemic veins in the right atrium. On the whole, pulmonary seizure is usually localized in the lower lobes; extralobar seizure most often affects the left lower lobe. Only in 10% of cases, extralobar seizure can be located infradiafragmatically. [24]

On radiography of the thorax, pulmonary seizure occurs as a triangular opacity with net and lobular edges, and if superinfected it has heterogeneous structure by the presence of cystic spaces. CT examination with contrast substance clearly illustrates systemic arterial intake. The key to the diagnosis is homogeneous iodophilia of a tissue mass similar to iodophilia of the aorta. An overinfected lung seizure has a more heterogeneous structure with airy or liquid cysts.

Inflammatory pseudotumor

Inflammatory pseudotumor is a reactive lesion consisting of inflammatory cells and fusiform myofibroblastic cells. Many terms have been used to describe this lesion,

including plasmocytic cell granuloma, fibrous histiocytoma, inflammatory myofibroblastic tumor or xantogranuloma.

Inflammatory pseudotumor can occur anywhere in the body, but the most common locations are the lung and orbital region. Clinically, patients may be asymptomatic or complain of coughing, hemoptysis, a history of infection, weight loss, fever or fatiguability.

As for the imaging features, inflammatory pseudotumor most often occurs as a nodule or solitary lung mass, up to 10 cm in diameter, with well-defined edges; sometimes it may have spiculated edges. [25] It may have a homogeneous or heterogeneous structure by the presence of hemorrhage, necrosis or calcifications. The type of iodophilia may vary. Adenomegaly and cavitation are less common.

2.4.4. Conclusions

In conclusion, the correct differentiation between lung lesions as benign or malignant is essential in patient management. There is a wide range of lung damage that can mimic the lung neoplasm. However, some of them exhibit certain key imaging features that help in differentiating from malignant lesions. Understanding the etiology, pathology, radiological characteristics and clinical course of these lesions, in general, is important in order not to interpret them as malignant lung tumors, which leads to unnecessary performance of lung biopsies.

2.5. Study of predictive factors of complications in imaging-guided pulmonary biopsies

2.5.1. Introduction

THE OBJECTIVE OF THE STUDY was to comparatively analyze the complication rate of percussive pulmonary biopsies and percutaneous biopsies from other organs, for a better preprocedural evaluation.

2.5.2. Materials and methods

Sampling procedures

This is a retrospective unicentric study that involved patients who were performed with percussive biopsies under CT guidance and ultrasound guidance in the Department of

Radiology of the Central Military Emergency University Hospital "Dr. Carol Davila" between March 2015 and October 2018.

The study is approved by the hospital's ethics committee. Patients were informed about possible complications including those related to their particular situation and signed an informed consent before each procedure, including for the processing of personal data for medical purposes.

For this study, we have not implemented a systematic sampling plan. The patients arrived in our clinic through intra- or interhospital consultation from oncologists or other medical specialties. They were asked to consult a recent CT/MRI/PET-CT investigation. Otherwise, they were carried out in our clinic. At the clinic, a primary radiologist evaluated the imaging of patients to confirm the suspicion and indication of the procedure. The same doctor designed the trajectory of the needle, taking into account safety and accuracy criteria. The CT scanner and ultrasound device used in the study were phillips brilliance 64 and GE LOGIQ P9, respectively.

Statistical study

The statistical study was conducted using IBM SPSS Statistics (Version 20). To compare the relationship between complications and biopsied organs, we selected the study population by type of biopsy organ and divided them into two groups: percutaneous pulmonary biopsies and percutaneous biopsies performed on the other organs. The "t" test of independent samples looked at statistical differences between the two groups for complications and other information such as clinical or procedure-related ones.

We used descriptive statistics to assess the number of complications and their rate for each organ and the Pearson correlation coefficient to describe the strength of the relationship between organ type and complications. We also explored the correlation between complications and the need for intervention with clinical information and procedure-related information.

2.5.3. Results

The largest number of procedures were performed on the lungs (n = 355), followed by breast biopsies (n = 70) and liver (n = 45). We divided the cases into two groups, percutaneous pulmonary biopsies (n = 355) and the other biopsies (n = 203).

There were 43 post-procedure complications, with a total rate of 7.7%. The group with pulmonary biopsies had the most complications, in the number of 40 and a rate of 11.3% (complications / organ biopsies). The complication rate for the other groups of biopsies was 1.5%, with only 3 complications, one for each of the liver, breast and mediastinum. The complication rate for mediastinal biopsies stands out by 10%, one of the reasons being the low number of only 10 mediastinal biopsies. (Table 2.1)

Table 2. 1Complication rates and their correlations with biopsied organs

	Biopsies		Complications			
	N	%	N	%	r	p
Adenopathy	10	1.8%	0	0.0%	-.04	.357
Digestive Tract	1	0.2%	0	0.0%	-.01	.773
Liver	45	8.1%	1	2.2%	-.06	.151
San	70	12.5%	1	1.4%	-.09*	.035
Mediastin	10	1.8%	1	10.0%	.01	.784
Bone	33	5.9%	0	0.0%	-.07	.087
Soft Parts	20	3.6%	0	0.0%	-.06	.189
Peritoneal	2	0.4%	0	0.0%	-.02	.683
Lung	355	63.6%	40	11.3%	.18**	< .001
Renal	2	0.4%	0	0.0%	-.02	.683
Retroperitoneal	7	1.3%	0	0.0%	-.03	.443
Splenic	1	0.2%	0	0.0%	-.01	.773
Adrenal	2	0.4%	0	0.0%	-.02	.683
Total	558		43	7.7%		

*The correlation is significant at 0.05 (2-tailed).

** The correlation is significant at 0.01 (2-tailed).

We calculated the Pearson correlation coefficient to assess the relationship between the type of biopsyd organ and postprocedural complications. The results indicated a relatively typical positive relationship between percutaneous pulmonary biopsies and the occurrence of complications (r (556) = .18, p <,001) and a small negative relationship between percutaneous breast biopsies and the occurrence of complications (r (556) = -.089,

p = .035). No other significant association was found between the occurrence of complications and the other biopsied organs.

The most common complication was pneumothorax, with 31 occurrences, of which 29 from lung biopsies with a rate of 8.1% and one each for the mediastinum and liver (0.9%).

The Pearson correlation coefficient was used to examine the relationship of complications and post-procedure interventions with clinical and procedural variables. The results indicated small positive correlations between the occurrence of complications and the use of CT guidance (r (487) = .15, p = .001) and repeated procedures (r (538) = .17, p <.001); small negative correlations of the histopathological diagnosis (r (522) = -.17, p <.001) with the INR (r (524) = -.10, p = .019). We were expecting a correlation between complications and interventions and a relatively large one was observed (r (339) =, 49, p <,001). No other statistically significant correlations were observed. In general, post-procedure complications are strongly correlated with emergency interventions. CT guidance, repeated procedures and a low INR correlate with the occurrence of complications, and the occurrence of complications is correlated, but not statistically significant, with the non-confirmation of histopathological diagnosis. (Table 2. 2)

Table 2. 2 Correlations between complications and clinical and procedural variables

	Complications		
	r	p	N
Age	.04	.321	556
Imaging Guide	.15**	.001	489
Gauge Ac	.09	.101	356
Intervention	.49**	< .001	541
Histopathological diagnosis	-.17**	< .001	524
Repeated procedure	.17**	< .001	540
Smoker	.01	.888	143
Obesity	-.08	.434	92
Diabetes mellitus	.02	.697	423
Hypertension	-.05	.448	212
INR	-.10**	.019	526

Glucose	.03	.563	517

* The correlation is significant at 0.05 (2-tailed).

** The correlation is significant at 0.01 (2-tailed).

* The correlation is significant at 0.05 (2-tailed).

The group of percutaneous pulmonary biopsies (N = 355) was associated with an occurrence of complications M = .11 (SD = .32). By comparison, the other group of percutaneous biopsies (N = 203) was associated with a occurrence of complications smaller numerically M = .01 (SD = .12). In order to test the hypothesis that pulmonary biopsies and biopsies from other organs were associated with different, statistically significant, averages of the occurrences of complications, an independent test of t samples was performed. The assumption of the homogeneity of variations was tested and was not satisfied by Levene's F test, F (556) = 87, p <.001. The test t of independent samples was associated with a statistically significant effect, t (501) = 5,2, p <001. Thus, pulmonary biopsies were associated with a statistically significant average occurrence of complications higher than other biopsies. Cohen's D was estimated at 0.37, which is an average effect. [26] (Table 2. 3)

Table 2. 3 Comparing the averages of the clinical and procedural variables of the two groups

	Lung		Old organs					
	M	SD	M	SD	t	df	p	Cohen's d
Complications*	0.1	0.3	0.01	0.1	5.2	501	< .001	0.37
Sex*	1.3	0.4	1.5	0.5	-6.47	383	< .001	-0.59
Age*	65	10.1	59.3	13.3	5.28	333	< .001	0.5
Imaging Guide*	0.8	0.4	0.3	0.5	11.59	224	< .001	1.26
Gauge Ac*	17.9	0.4	17.6	1.6	2.42	160	.01	0.30
Complications with Intervention*	0.03	0.2	0.01	0.1	2.27	516	.02	0.17
Smoker*	0.9	0.3	0.7	0.5	1.57	21	.13	0.49
Obesity*	0.3	0.4	0.5	0.5	-1.93	50	.06	-0.45
Diabetes Mellitus**	0.2	0.4	0.2	0.4	-0.45	421	.65	-0.05
Hypertension**	0.7	0.5	0.7	0.5	0.01	210	.99	0
INR**	1.1	0.1	1.1	0.1	-0.01	524	.99	0

Blood glucose**	111.4	41	109.2	39.9	0.6	515	.55	0.06
Systolic Tension*	131.1	13.3	127.7	20	0.81	33	.43	0.22

* Equal variations not assumed.

** Equal variations assumed.

2.5.4. Discussions

The complication rate of lung biopsies obtained in this study is 11.3%, statistically higher than the other biopsies that had a complication rate of 1.5%. The difference between moderate-major complication rates (those in need of emergency intervention) between the two groups is statistically significant, with a rate of 2.8% for lung biopsies and a rate of 0.5% for the other group. In our study, the most common complication is pneumothorax, with a rate of 8.1% of lung biopsies and 0.9% of other biopsies. Pneumothorax as a moderate-major complication has a rate of 2.5%, with 9 cases out of 31 requiring the placement of a pleural drainage tube. The other complications that required intervention were hemotorax (n = 1) and infection (n = 1) for lung biopsies and superficial hematoma (n = 1) for the other group. The second most common complication is hemorrhage (n = 9), which did not require blood transfusion.

The complication rate for both groups falls within the limits reported in the literature. [27,28] Previous studies and meta-analyses of percutaneous biopsies and complications reported pneumothorax and hemorrhage/hemoptysis as common complications. Pneumothorax is reported, on average, with a rate of 20%, and with a rate of 6.6% of placement of the drainage tube. Hemorrhage is found in 1% and only 0.1% requires intervention. [2,29,30]

From our experience we can argue that the key element that influences the higher rate of complications is the use of CT guidance, this is used in cases with higher difficulty, where the lesion is located more centrally; thus, several pleural surfaces are punctured, and also the lesion is located near the larger blood vessels. [31]

2.5.5. Conclusions

Percutaneous pulmonary biopsies have a statistically higher complication rate compared to biopsies from other organs, although it is a widely accepted procedure with relatively few complications. In conclusion, percutaneous pulmonary biopsy is riskier and more expensive than biopsies performed from other organs. The risk is especially higher

when performed under CT guidance, this being especially true in cases considered more difficult. Percutaneous pulmonary biopsy should be avoided when a biopsy is available in another organ with the same pathological context. Lung injury requires precise planning and detailed knowledge of both interventional radiology and diagnostic radiology to avoid unnecessary complications.

2.6. Study of diagnostic accuracy of percutaneous pulmonary biopsies

2.6.1. Results

The statistical study was performed on 52 pulmonary biopsies collected from patients aged between 43 and 86 years, which were distributed in 3 age groups.

Of the 52 cases, 44 (84.61%) had a diagnosis of malignancy, and 8 cases (15.39%) were non-diagnostic. Regarding the size of the fragments, only in one case of those with a maximum size >10mm was the suspicion of malignancy refuted. The relatively small number of samples analysed (52) makes this association not statistically significant, but may be a cornerstone for further studies. Also, a greater number of biopsy fragments at the confirmation of the radiological diagnosis of malignancy, in 100% of the cases in which 4 fragments were collected and 86.2% of the cases in which the >5 fragments were collected.

Non-diagnostic biopsies can be subclassified into: nonspecific histopathological aspect (3 cases, 37.5%), marked necrosis with histopathological characters insufficient for malignancy (2 cases, 25%), infectious processes (2 cases, 25%) and inflammation (1 case, 12.5%).

Following the histopathological examination and immunohistochemical tests performed on the biopsy materials, a number of 9 pulmonary metastases were revealed, 7 of them (77,7%) being attributed to the female sex.the sex of the patients is statistically significant correlated with the diagnosis of pulmonary metastasis, with a value $p<0.05$ ($p=0.036$).

Well-differentiated adenocarcinomas G1 (1 case of metastasis from adenocarcinoma colo-rectally and 1 case of pulmonary metastasis from pancreatic ductal adenocarcinoma) and moderately differentiated ones G2 (1 case of colo-rectal adenocarcinoma metastasis and 2 cases of metastases from bilio-pancreatic tract adenocarcinomas) have been associated more frequently with pulmonary metastases than poorly differentiated adenocarcinomas G3 (16 cases of primary lung tumors and 1 case of metastasis from

endometrial adenocarcinoma) have been associated more frequently with pulmonary metastases than poorly differentiated adenocarcinomas G3 (16 cases of primary lung tumors and 1 case of metastasis from endometrial adenocarcinoma poorly differentiated endometrioid G3), statistically significant aspect, with a value p=0.035.

However, lymphovascular invasion and tumoral alveolar diffusion (STAS) were better represented in the case of poorly differentiated primary pulmonary and secondary G3 adenocarcinomas (12/17 cases, of which 11 primary, respectively 70.5% of poorly differentiated primary adenocarcinomas with lympho-vascular invasion and 3/17 cases with STAS), which suggests an increased risk of remote metastasis and loco-regional recurrence, with statistical significance with $p<0.0001$ in case of lympho-vascular invasion.

2.6.2. Discussions

Imaging-guided biopsies both CT and ultrasound are used and necessary for the diagnosis of pathological tumor masses and the establishment of a subsequent therapeutic plan.

The purpose of this audit is to evaluate the performance of Dr. Cezar Bețianu regarding the quality of pulmonary biopsies performed imaging over a period of 12 months.

Biopsies collected by needle-tricked needle biopsy increase the rate of positive diagnosis according to specialized studies from 52% to 91%. [32–37]

The role of biopsy is to assess histopathologically, immunohistochemically and molecular tumor histological subtypes and not cells compared to aspiration biopsies. [32,36]

According to studies in the literature, biopsies smaller than 10 mm have a higher rate of false negatives for malignancy, which supports the importance of obtaining tissue materials through this technique. [38]

And in our study, the small size of the harvested fragment was associated with a false negative result.

In this study, the number of biopsies did not statistically correlate with nondiagnostic results, most likely due to the small number of patients included in the study.

In some studies, in small lesions ranging in size from 15 mm to 20 mm, the rate of diagnostic accuracy increased from 84% to 88% in the case of 2.5, respectively, 3 biopsies per lesion. [36,39]

Tsukada et al found a 67% accuracy rate for lesions below 10 mm for an average of 1.4 biopsies per lesion. [40]

The purpose of this study was to evaluate the achievement of a definitive diagnosis by morphological aspects with or without immunohistochemical testing.

The diagnostic concordance in the subtypes of non-small cell lung carcinomas in our study was similar to other publications. [41]

The biopsy fragments large enough and many in number allow the establishment with certainty of some important factors involved in the diagnosis and prognosis of the patients such as the histological degree, the lymphovascular invasion, the histological subtype as well as the establishment of the injured origin with the help of a restricted antibody panel to allow further molecular testing.

It was also possible to evaluate an independent prognostic factor according to the new WHO Criteria, tumor alveolar difusion.

2.7. Conclusions and personal contributions

Percutaneous biopsy is a high-profile safety procedure, taking in consideration the selection of patients by clinical study and imaging.

The positive predictive value of trucut needle biopsy is very high and has a major influence on patient management.

CT imaging guidance is associated with higher rates of complications, on the one hand by addressing more difficult cases with central nodules, on the other hand by the difficulties of the technique. Fluoroscopic CT guidance is more advantageous but it is still difficult to access. Ultrasound guidance is fast and reliable, it can be used on most organs and is associated with a lower rate of complications.

Addressing lung lesions requires careful planning and the use of detailed technical and anatomical knowledge to avoid unnecessary complications and limit the rate of major complications.

Lung biopsy is associated with a higher rate of complications compared to biopsies in other organs and can lead to higher costs through prolongation of hospitalization and the need for additional interventions. Even so, it can be used as an alternative for surgical biopsy in advanced cases.

Pneumothorax is the most common complication of lung biopsies and is the complication with the most common therapeutic interventions.

The prevalence of complications of these lung biopsies could be decreased by choosing another organ for biopsy, when feasible.

Another way to reduce prevalence can be by avoiding biopsies from lesions that mimic the imaging aspect of the lung neoplasm. These lesions have typical imaging appearance most of the time. The experience and alertness of the radiologist helps to differentiate them from malignant lesions.

INR values have a counterintuitive association with the rate of complications, in the sense that higher values are associated with fewer complications. This can be explained by the sealing effect of hematic products on pneumothorax, but it is worth further investigation.

2.8. Selective bibliography

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