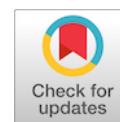


ORIGINAL ARTICLE



# Clinicopathological characteristics of pulmonary nodules: Experience at Clínica Reina Sofia, Bogotá, Colombia

## Características clinicopatológicas de nódulos pulmonares: Experiencia en Clínica Reina Sofia, Bogotá, Colombia

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### Abstract

**Introduction.** Lung cancer is the leading cause of cancer mortality worldwide, which makes it a public health problem. There are different imaging findings that suggest the presence of lung cancer, one of which is pulmonary nodules; however, these can also be seen in benign entities.

**Methods.** A total of 66 patients with pulmonary nodule biopsy at Clinica Reina Sofia, in the city of Bogota D.C. were included between March 1, 2017 and February 28, 2020. The demographic characteristics of the patients, the morphologic and histopathologic characteristics of the pulmonary nodules and their correlation with their pathological diagnosis were analyzed.

**Results.** 69.2% of the nodules studied had malignant etiology, of these 55.5% were of metastatic origin, and 44.5% were primary lung neoplasms, with a solid pattern in 70.6% of the cases. The most frequent histological pattern was adenocarcinoma. Regarding the radiological characteristics, most of the malignant nodules measure 1 to 2 cm, of smooth morphology and had multiple distribution, located in the upper lobes.

**Conclusions.** The characterization of pulmonary nodules provides relevant information that guides the most frequent diagnoses in our setting, when suspicious nodules found incidentally or in the follow-up of another tumor are studied. As the nodule is the manifestation of early lung cancer, establishing screening programs that allow timely diagnosis is now an urgent need to reduce mortality.

**Keywords:** lung neoplasms; solitary pulmonary nodule; needle biopsy; pathology; diagnosis; diagnostic imaging.

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## Resumen

**Introducción.** El cáncer de pulmón es la primera causa de mortalidad por cáncer a nivel mundial, lo que hace que sea considerado un problema de salud pública. Existen diferentes hallazgos imagenológicos que hacen sospechar la presencia de cáncer de pulmón, uno de los cuales son los nódulos pulmonares; sin embargo, estos también pueden verse en entidades benignas.

**Métodos.** Se incluyeron 66 pacientes con biopsia de nódulo pulmonar en la Clínica Reina Sofia, en la ciudad de Bogotá, D.C., Colombia, entre el 1° de marzo del 2017 y el 28 de febrero del 2020. Se analizaron las características demográficas de los pacientes, las características morfológicas e histopatológicas de los nódulos pulmonares y la correlación entre sus características imagenológicas e histopatológicas.

**Resultados.** El 69,2 % de los nódulos estudiados tenían etiología maligna, de estos el 55,5 % era de origen metastásico y el 44,5 % eran neoplasias primarias de pulmón, con patrón solido en el 70,6 % de los casos. El patrón histológico más frecuente fue adenocarcinoma. Respecto a las características radiológicas, en su mayoría los nódulos malignos median de 1 a 2 cm, de morfología lisa y distribución múltiple, localizados en lóbulos superiores.

**Conclusiones.** La caracterización de los nódulos pulmonares brinda información relevante que orienta sobre los diagnósticos más frecuentes en nuestro medio, cuando se estudian nódulos sospechosos encontrados incidentalmente o en el seguimiento de otro tumor. Como el nódulo es la manifestación del cáncer temprano del pulmón, establecer programas de tamización que permitan el diagnóstico oportuno, es hoy día una imperiosa necesidad, para reducir la mortalidad.

**Palabras clave:** neoplasias pulmonares; nódulo pulmonar solitario; biopsia con aguja; patología; diagnóstico; diagnóstico por imagen.

## Introduction

Lung cancer currently represents the main cause of cancer mortality worldwide and according to the Globocan 2020 report, the annual incidence is approximately 2.2 million people, which makes it considered a public health problem.<sup>1,2</sup> In Colombia, an approximate prevalence of 27.2 per 100,000 inhabitants is estimated, with an incidence rate calculated in men of 36.5 and in women of 19.9 per 100,000 inhabitants, corresponding to the third cause of death from cancer in men and the fifth in women<sup>2,3</sup>.

Smoking has been identified in 90% of cases as the main risk factor for the development of lung cancer<sup>4-7</sup>. It has been estimated that the risk of developing lung cancer in a smoker is 20 times higher than in a non-smoker. The incidence increases with age, exposure to other carcinogenic agents such as radon, asbestos, exposure to radiotherapy, pulmonary fibrosis, genetic factors, a history of chronic obstructive pulmonary disease, alcohol use and HIV infection, among others<sup>8-13</sup>.

Clinically, early stages can go unnoticed due to the absence of symptoms or signs, which is why an active search is necessary with screening programs in patients at high risk for lung cancer and the simultaneous implementation of prevention strategies in which modifiable risk factors are intervened, such as smoking cessation.

There are different radiological findings that suggest the presence of lung cancer, and one of these is pulmonary nodules. These have been defined as opacities with a diameter of 3 centimeters or less, surrounded by lung parenchyma, may be single or multiple, solid or subsolid, and may be located in one or both lungs. Lesions larger than 3 centimeters are called masses and are more likely to be malignant. The characteristics of the nodule and the patient's risk factors lead us to suspect that a nodule is malignant or not.

Its radiological evaluation by computed tomography (CT) has allowed a better characterization of the nodules<sup>13-15</sup>. However, there is currently no consensus about its management and follow-up,

which makes accurate diagnosis difficult and favors delayed diagnosis<sup>4</sup>. This implies presentations in advanced stages, which impacts not only treatment but also prognosis, with a consequent increase in the economic burden of the disease<sup>16-20</sup>.

The purpose of this study was to describe the results obtained in our institution when correlating the clinical and radiological characteristics of the pulmonary nodules with the histopathological results, in a cohort of patients with imaging findings of suspicious pulmonary nodules, who underwent biopsy using a multidisciplinary approach.

## Methods

For the present study, all patients older than 18 years were included, with pulmonary nodules who, in the pathology records of the Clínica Reina Sofia, in Bogotá, Colombia, had a biopsy of a pulmonary nodule by any method, between March 1, 2017 and February 28, 2020. Patients with incomplete records in the clinical history were excluded.

The data was collected retrospectively. The clinical-radiological, histological and pathological characteristics of the lesions and the diagnostic methods used were analyzed, whether they were transbronchial or percutaneous biopsy or surgical resection (wedges or anatomical resections).

An analysis was performed to describe the characteristics of the sample, the quantitative variables were analyzed through measures of central tendency and dispersion; categorical data using frequencies and proportions. The assumptions of normal distribution in the variables of interest were evaluated with the Shapiro-Wilk test and through graphical analyzes (frequency histograms and Q-Q graphs).

The patients were classified into two groups, with malignant pathology or with benign pathology, for the corresponding analysis of the radiological characteristics. To calculate the proportion of successful non-surgical biopsies (those performed through bronchoscopy or percutaneous biopsies), the proportion of successful non-surgical biopsies among the total number of non-surgical biopsies performed was determined. Mortality and complications were expressed as the total number of

patients who presented the event (mortality or complication) within 30 days after surgery. The patients were evaluated during follow-up that took place approximately between 7 and 15 days after the procedure.

Pulmonary nodules were characterized by their location, size, borders and the presence of calcifications or fat, stability or growth; the classification that divides them into solids and subsolids<sup>9</sup> was used, the latter subdivided into ground glass nodules and partially solids, previously called heterogeneous or mixed.

## Results

### *Patient demographics*

A total of 70 patients who met the inclusion criteria were selected, and of these, four were excluded because they did not have a complete clinical history that would allow analysis. A total of 66 patients were eligible to be included in the analysis, in whom the presence of at least one pulmonary nodule was identified by imaging studies and subsequently underwent histopathological confirmation.

Of the 66 patients, 38 were female (57.5%), the average age was 68.1 years with a standard deviation of 13.6 (range: 24-89) (Table 1). A total of 35 patients (53.0%) had a known diagnosis of oncological pathology and 41 patients (62.1%) had a family history of oncological pathology at the time of identification of the pulmonary nodule. Other patients' history included arterial hypertension in 32 patients (48.4%), diabetes mellitus in eight patients (12.1%), and pulmonary disease in nine patients (13.6%). Another relevant antecedent found in the patients was the smoking habit in 23 patients (34.8%).

Within the clinical characteristics, the presence of symptoms was found in half of the patients, with cough (36%) being the predominant symptom, followed by chest pain (14%), dyspnea (11%) and weight loss (6.3%).

Histopathological analysis showed malignant nodule in 69.2% and benign in 30.7%. Of the 45 malignant nodules, 55.5% were of metastatic origin and 44.5% were primary lung tumors (Ta-

**Table 1.** General characteristics and relevant background of the studied sample.

	n	%
Age (Range)	69 (24- 89)	
Sex		
Female	38	57.5
Male	28	42.5
Family history of cancer	41	62.1
Pathological personal history		
Oncological	35	53.0
Arterial hypertension	32	48.4
Diabetes mellitus	8	12.1
Chronic obstructive pulmonary disease (COPD)	5	7.6
Other lung diseases	4	6.0
Heart disease	4	6.0
Collagen disease	2	3.0
Chronic kidney disease	2	3.0
Other relevant history		
Smoker	23	34.8

**Table 2.** Histological diagnosis of pulmonary nodules.

Histological Behavior	n	%
Benign	20	30.7
Inflammatory	9	45
Infectious	6	30
Benign tumor	5	25
No evidence of malignancy	7	
New biopsy	6	
Observation	1	
Malignant		
Metastasis	45	69.2
Gastrointestinal	25	55.5
Breast	9	20
Sarcoma	5	11.1
Genito-urinary	3	6.6
Lymphoma	2	4.4
Prostate	2	4.4
Fusocellular	1	2.2
Gynecological	1	2.2
Parotid	1	2.2
Primary	1	2.2
Adenocarcinoma	20	44.5
Acinar	17	85
Solid	10	50
Lepidic	2	10
In situ	2	10
Minimally invasive	2	10
Neuroendocrine	1	5
Squamous cell	2	10
Escamocelular	1	5

ble 2). The origin of the metastases in order of frequency was gastrointestinal 20% (with predominance of the colon and rectum), breast 11.1%, and sarcomas in 6.6%. In the 20 patients where the malignant nodule corresponded to a primary lung tumor, the most frequent diagnosis was adenocarcinoma in 85% (17/20).

The nodules were multiple in 57.5% and the most frequent locations were the upper lobes, with 12.1% each. According to the type of nodule, it was solid in 77.2%, partially solid in 12.2%, and ground glass in 10.6%. Other radiological characteristics of the nodule are described in Table 3.

An additional analysis that compared the size of the nodule with the percentage of success of the biopsies showed a success rate of 40% in nodules from 1 to 2 cm and 75% in those larger than 2 cm for the percutaneous procedure; on the other hand, in transbronchial biopsies, success was 66.7% (2/3) in patients with nodules larger than 2 cm, corresponding to one patient with sarcoma and another with metastatic gastrointestinal adenocarcinoma (Table 4).

When analyzing the 20 nodules with benign histology, 45% were found to be inflammatory lesions, 30% infectious, 25% benign tumors and seven patients without evidence of malignancy, six of whom were subsequently taken to surgical biopsy for definitive histological diagnosis, taking into account that prior to this surgical intervention had imaging characteristics suspicious for malignancy, and the results obtained were an adenoleiomyomatosis and two fibrous tumors of the pleura.

The patient with the inconclusive biopsy, who did not accept a second intervention for histological confirmation, has had approximately two years of radiological follow-up and has not presented changes in the morphology and size of the pulmonary nodule (Figure 1).

When comparing the type and characteristics of the nodule according to histological behavior (malignant or benign), it was found that solid (70.6%) and ground glass (71.4%) nodules are more frequently malignant, while partially solid were malignant in 50% of cases.

**Table 3.** Clinical features of pulmonary nodules.

	n	%
Patient has symptoms	34	51.5
Evolution of patients		
Initial study of nodules	51	77.2
Nodule enlargement	11	16.6
Appearance of new nodules	3	4.5
No data	1	1.5
Number of nodules		
Multiple	38	57.5
Solitary	28	42.5
Location of nodules		
Multiple lobes	36	54.8
Right upper lobe	8	12.1
Left upper lobe	8	12.1
Middle lobe	5	7.5
Left lower lobe	5	7.5
Right lower lobe	4	6.0
Nodule type		
Solid	51	77.2
Partially solid	8	12.2
Ground glass	7	10.6
Characteristics of the nodule		
Smooth	22	33.3
Spiculated	19	28.7
Lobed	19	28.7
Cavitated	5	7.6
Calcified	1	1.5
Nodule size		
Less than 1 cm	12	18.1
1 to 2 cm	38	57.5
Greater than 2 cm	16	24.2

According to the morphological characteristics of the nodule (Table 5), the malignant ones predominated with a higher percentage in the lobulated ones in 84.2% (16 patients) and the cavitated ones in 80% (4 patients), while the smooth border was the most predominant characteristic among benign nodules, with nine patients out of 21 (40.9%).

The type of nodule according to the histopathology of primary lung tumor was also compared, finding that adenocarcinomas are mainly solid (58.8%), and to a lesser extent ground glass (23.5%) or part solid (17.7%). All neuroendocrine and squamous cell tumors showed a solid pattern (Table 6).

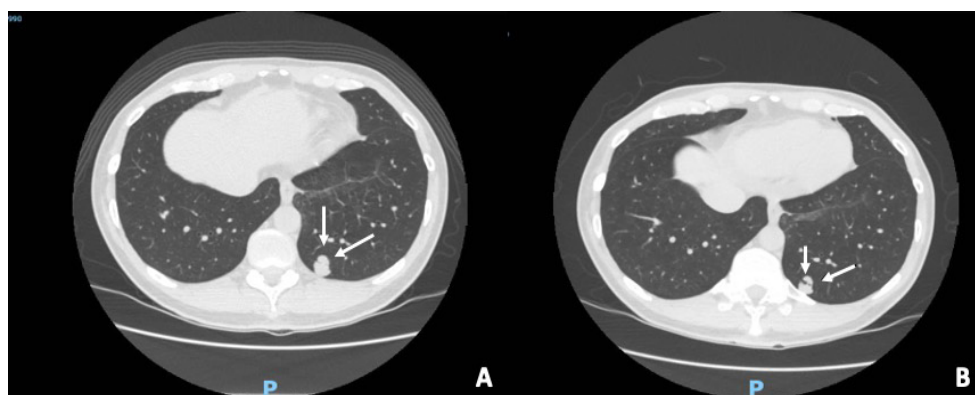
Within the aspects related to the diagnosis, it was found that for the first approach, the most frequently performed procedure was surgery (78.9%), followed by percutaneous biopsy (15.1%) and transbronchial biopsy (6%) (Table 7). The diagnostic success of non-surgical biopsies was 50%; in the other 50%, corresponding to seven of 14 patients in whom the diagnosis was not achieved, in six a surgical biopsy was performed as a second procedure, to obtain histological confirmation, and the remaining patient was left under observation.

The average length of hospital stay was 2.9 days (range 1-13). There were no intraoperative complications, but in 6% of patients there were minor complications after surgery, which did not require additional major reoperation, consisting of an alveolar-pleural fistula that caused subcutaneous emphysema, with persistent air leak in three patients (one of these in combination with

**Table 4.** Comparison of the size of the nodule with the performance and success of non-surgical biopsy.

	Percutaneous biopsy n=10		Transbronchial biopsy n=4	
	All	Success	All	Success
Nodule size				
Less than 1 cm	1 (9.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
1 to 2 cm	5 (54.5%)	2 (40%)	1 (25.0%)	0 (0.0%)
Greater than 2 cm	4 (36.4%)	3 (74.6%)	3 (75.0%)	2 (66.7%)





**Figure 1.** Patient in follow-up of pulmonary nodule. A. Computerized axial tomography of the year 2018, where a nodule (arrows) was identified, to which a percutaneous biopsy was performed, with a negative pathology report for malignancy. B. Imaging findings of the same pulmonary nodule at 2 years of follow-up, with no changes compared to the previous study.

**Table 5.** Anatomical characteristics of the nodule according to benign or malignant behavior.

	Malignant n=45	Benign n=21*
Characteristics of the nodule		
Smooth	13 (59.1%)	9 (40.9%)
Spiculated	12 (63.5%)	7 (35.5%)
Lobed	16 (84.2%)	3 (15.8%)
Cavitated	4 (80%)	1 (20%)
Calcified	0 (0.0%)	1 (100%)

\*20 confirmed by histology and one that is assumed by follow-up.

**Table 6.** Behavior of the type of nodule according to histopathology of primary lung tumors.

	Adenocarcinoma n=17	Neuroendocrine n=2	Squamous cell n=1
Nodule type			
Solid	10 (58.8%)	2 (100%)	1 (100%)
Partially solid	3 (17.7%)	0 (0.0%)	0 (0.0%)
Frosted glass	4 (23.5%)	0 (0.0%)	0 (0.0%)

pneumothorax with prolonged chest tube requirement) and another patient with pneumothorax less than 30%, which did not affect ventilatory mechanics.

Continuous monitoring was required in the intensive care unit in four patients (6%), two of

**Tabla 7.** Aspectos relacionados con el diagnóstico y evolución intrahospitalaria de los pacientes.

	n	%
Procedure performed 1st approach		
Surgery	52	78.7
Percutaneous Biopsy	10	15.1
Transbronchial biopsy	4	6
Diagnosis by 1st approach	59	89.4
Requires ICU in the Postoperative	4	6.0
Complications	6	9.0
Minor (Alveolopleural Fistula)	4	6.0
Major (Shock pop)	2	3.0
None	60	91.1
Days of hospital stay Me (Range)	2 (1 - 13)	
Mortality	2	3.0
Histological Behavior		
Malignant	45	68.1
Benign	21	31.9

them with major complications (2.9%) that led to mortality and the other two due to the need for postoperative surveillance, one of these with respiratory acidosis and mild hyperlactatemia after the procedure, and another 82-year-old female patient with multiple comorbidities who required a

median lobectomy, both patients with subsequent satisfactory evolution.

In relation to mortality, it occurred in two of the patients, the first an 86-year-old woman with carcinomatosis and malignant pleural effusion who underwent the diagnostic procedure in very poor general condition, presented electrical activity without a pulse in the immediate postoperative period and died few days later, and the second patient, a 76-year-old man in whom a lung wedge biopsy showed metastasis of known colorectal neoplasia, required ICU due to hemodynamic instability in the postoperative period and was operated on again 12 hours later, ruling out bleeding as a cause of his instability, who died on the tenth postoperative day despite not having surgical complications.

## Discussion

The finding of pulmonary nodules in imaging studies becomes a true diagnostic challenge for the physician and generates anxiety in the patient, considering that its etiology could be malignant. The appearance of lung cancer before the age of 30 is very rare and increases with age<sup>21-24</sup>. Pulmonary nodules in patients older than 70 years have shown a higher probability of malignancy<sup>25,26</sup>, including lung cancer. In our study, a mean age in the late seventh decade of life was identified, similar to that described by other authors<sup>27,28</sup>.

The estimated frequency of the etiology of pulmonary nodules varies substantially between studies, reflecting differences between study populations and the methodology used to establish a diagnosis. However, even early detection studies in smokers at high risk of malignancy find that the vast majority of nodules identified on computed tomography are benign. For example, in the Pan-Canadian Early Detection of Lung Cancer and British Columbia Cancer Agency studies, among the 12,029 nodules found, only 144 (1%) were malignant [13]. Taking these results into account, it could be inferred that the incidence of malignant nodules is much lower in patients with medium or low risk of lung cancer.

In the present study, a frequency of malignant nodules of 68.1% was found, despite the low fre-

quency of smoking. Two determining aspects must be taken into account: first, it is a population of nodules selected for biopsy because they are considered suspicious after being evaluated by experts and some of them followed for some time and, second, most of the patients had some personal history or family cancer, which increases the risk of having a malignant nodule.

Lee et al<sup>27</sup> show a predominance of the appearance of pulmonary nodules in men, which differs from what was found in the present study, which showed a higher frequency in women, similar to other studies<sup>26</sup>.

Spiculated borders and the location of a nodule in the upper lobes have been related to primary lung malignancy<sup>13,29</sup>, however, inflammatory or infectious pathologies can also be seen as spiculated nodules<sup>17,30,31</sup>. The malignancy of the spiculated nodules included in this study was 63.5%, but it should be noted that the morphological characteristic of the lobulated nodule was the predominant within the group of malignant etiology, with more than 84%.

In addition, solid-type nodules were the most frequent, in 77% of patients, being the most frequent pattern, both in benign and adenocarcinomas. The ground glass pattern was observed in adenocarcinoma in situ, minimally invasive, and predominantly lepidus. This is why it is important to carry out an adequate differentiation of the nodules, since the recognition of a subsolid morphology, especially the partially solid ones, has a significantly higher risk of malignancy, when compared to the solid ones, especially, special attention should be paid if subsolids develop changes in size, or the solid component appears or increases. As a relevant piece of information, the slight predominance of neuroendocrine tumors over squamous cell tumors was striking, probably because it was mostly the study of peripheral pulmonary nodules<sup>32</sup>.

In a patient with known extrathoracic malignancy, the probability of malignancy of a pulmonary nodule identified on a chest radiograph is approximately 25%<sup>33</sup>. These nodules are generally not considered incidental, since they are found in the follow-up of another neoplasm

that can potentially metastasize to the lung. In our study, we identified a predominance of metastatic pulmonary nodules from gastrointestinal and breast carcinoma, which are two of the malignant pathologies that progress very frequently with pulmonary dissemination. Classically, metastatic nodules have been described as multiple nodules with smooth borders, and in this study, 20 of the 25 patients with metastatic nodules (77%) had these characteristics.

The most common cause of benign pulmonary nodules includes granulomatous infections and benign tumors such as hamartomas, and less common causes include vascular and inflammatory lesions<sup>28</sup>. In our study, benign nodules of inflammatory and infectious etiology were identified more frequently, with a lower proportion of benign tumors. Similarly, the borders of the benign nodules were mostly represented smooth and spiculated, which agrees with what was reported by Vega *et al.*, in a study of the Chilean population<sup>28</sup>.

The bronchoscopy diagnostic sensitivity to obtain a histological diagnosis in a pulmonary nodule varies from 20 to 80%, depending on the size of the nodule, its proximity to the bronchial tree, and the prevalence of cancer in the study population. For nodules less than 1.5 cm in diameter, the sensitivity is 10% and for those 2 to 3 cm, 40 to 60%<sup>31</sup>. Schwarz *et al* achieved a 41% diagnostic success rate using bronchoscopy biopsies in adults with solitary pulmonary nodules. In a meta-analysis of 54 studies, they analyzed the diagnostic performance of transbronchial biopsy in 7,285 nodules, which was 70.6%, and this performance was higher in malignant lesions larger than 2 cm, adjacent to a bronchus<sup>17</sup>. In our study, for transbronchial biopsy, a yield of 50% was obtained, being higher in nodules larger than 2 cm. However, it must be kept in mind that the sample of transbronchial biopsies is small, which limits the analysis of the results. However, in clinical practice we consider that very few transbronchial biopsies are performed, which means that

the experience of the operators is also limited, which can impact the results.

In percutaneous biopsies, the sensitivity and specificity reported by Zhang *et al*<sup>32</sup> were 95% to 100% and 70% to 93%, respectively. This percentage of effectiveness is similar to that of more recent studies, such as the one reported by Kiranantawat<sup>33</sup>, with diagnostic sensitivity and specificity for malignant nodules of 95 and 100%, respectively. Although we did not have such good results in our study, we do appreciate that, like transbronchial biopsies, the size of the nodule and the experience of the operator play a fundamental role in obtaining a better diagnostic performance.

What is important to note is that of the six cases in which a surgical biopsy was performed due to a negative percutaneous or transbronchial biopsy report for malignancy, three cases (50%) had malignant lesions and the remaining three had benign tumors that also required treatment. For this reason, it is very important to emphasize that a non-diagnostic biopsy cannot be misinterpreted as benign, but that another technique must be insisted on until an accurate diagnosis is obtained.

Lung cancer mortality could be reduced with early detection tests. Using the National Lung Cancer Screening Trial (NLST), it was shown that serial CT reduced lung cancer mortality by 20% in high-risk patients. Lung nodules, which were detected as an incidental finding in up to 25% of individuals on NLST, are an example of the benefit of these screening programs<sup>34</sup>. It is important to make greater efforts in our country to establish these screening programs, which help to identify pulmonary nodules that correspond to early-stage primary lung carcinoma and thus achieve a reduction in mortality from lung cancer. It is important to note that none of the nodules in this study were found in a screening program in patients at high risk for lung cancer, all were patients in whom CT was performed for a specific indication, follow-up of a neoplasm or incidentally in the study of a symptom or other concomitant pathology.



## Conclusions

The study of pulmonary nodules provides relevant information that guides the most frequent diagnoses in our population, when suspicious nodules found incidentally or in the follow-up of another tumor are studied.

Most of the nodules in this study were of malignant etiology, diagnosed in 68.1% of the samples analyzed histologically, since the population was limited to nodules considered suspicious and were sent for histological diagnosis, in a population that in more than 50% had already had an extrapulmonary primary tumor.

The information obtained should serve as motivation for future prospective, multicenter, more robust studies, with a greater number of patients, where other variables not included in this study due to their retrospective nature can be analyzed, in order to be able to know with greater certainty the characteristics of the nodules that we are submitting to histological diagnosis in our setting. It is necessary to implement screening methods for lung cancer with strategies that have shown a reduction in mortality in the susceptible population.

## Compliance with ethical standards

**Informed consent:** According to resolution 8430/1993, it is an investigation without risk because retrospective data are presented that do not modify the patient's behavior, so it does not require completion of informed consent. The study was carried out after the approval of the protocol by the research commission and the institutional ethics committee. It was carried out in accordance with the Declaration of Helsinki of 1975, promulgated by the World Medical Association and the observance of Resolution No. 008430/1993 of the Ministry of Health. The information was in the custody of the main investigator and the investigation protocol adhered to the statutory law of habeas data.

**Conflicts of interest:** The authors declare that they have no conflicts of interest.

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## Author's contributions:

Conception and design of the study, data acquisition, and data analysis: Stella Isabel Martínez, Alexander Fernández, Angie Carolina Riscanevo y Laura Escobar.

Data analysis, interpretation, and critical review: Stella Isabel Martínez y Alexander Fernández.

Final approval of the manuscript: Stella Isabel Martínez, Alexander Fernández, Angie Carolina Riscanevo y Laura Escobar.

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