

## **Histopathological tendencies, sex, age and radiological results for lung cancer in the municipality of Sinop – MT**

**Padrão histopatológico, gênero, idade e resultados radiológicos do câncer de pulmão no município de Sinop – MT**

**Patrón histopatológico, género, edad y resultados radiológicos del cáncer de pulmón en el municipio de Sinop - MT**

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### **Abstract**

*Objective:* To describe and improve our understanding of lung cancer epidemiology. *Methodology:* Retrospective, descriptive and analytic epidemiological study, analyzing histological type, sex, age and radiological results for lung cancer in the municipality of Sinop – MT during the period from 2014 to 2019. *Results:* 219 lesion biopsies were analyzed. 113 (51.59%) confirmed a diagnosis for lung cancer. The main histological types for the histopathology diagnosis were adenocarcinoma totaling 47 (41.59%) cases, followed by squamous cell carcinoma with 27 (23.89%) cases. Regarding sex, 52 (46.02%) lung cancer cases were found in women and 61 (53.98%) cases in men. In total, the main histological type for both sexes was adenocarcinoma. Regarding age, the predominant age range was 60-69 years with 43 cases (38.05%). In relation to characteristics of tomography imaging for lung cancer cases, nodule location was statistically significant, mainly in the right lung upper lobe, a finding observed in other sources, where the upper right lobe was found to have a greater incidence of malignancy. *Conclusions:* the main histological type was adenocarcinoma, with the majority of malignant lesions occurring in men, with an age range from 60 to 69 years. The most common image for cancer cases was solid lesion larger than 8 mm with irregular borders found in the right lung upper lobe.

**Keywords:** Lung neoplasms; Epidemiology; Histology; Tomography, X-ray computed; Neoplasms.

### **Resumo**

*Objetivo:* Descrever e aprimorar nossa compreensão da epidemiologia do câncer de pulmão. *Metodologia:* Estudo epidemiológico retrospectivo, descritivo e analítico, analisando tipo histológico, sexo, idade e resultados radiológicos para câncer de pulmão no município de Sinop – MT no período de 2014 a 2019. *Resultados:* Foram analisadas 219 biópsias de lesões. 113 (51,59%) confirmaram o diagnóstico de câncer de pulmão. Os principais tipos histológicos para o diagnóstico histopatológico foram adenocarcinoma totalizando 47 (41,59%) casos, seguido de carcinoma de células escamosas invasivo com 27 (23,89%) casos. Em relação ao sexo, 52 (46,02%) casos de câncer de pulmão foram encontrados em mulheres e 61 (53,98%) casos em homens. No total, o principal tipo histológico para ambos os sexos foi o adenocarcinoma. Em relação à idade, a faixa etária predominante foi de 60 a 69 anos com 43 casos (38,05%). Em relação às características da imagem tomográfica para casos de câncer de pulmão, a localização do

nódulo foi estatisticamente significativa, principalmente no lobo superior do pulmão direito, achado observado em outras fontes, onde o lobo superior direito apresentou maior incidência de malignidade. *Conclusão:* o principal tipo histológico foi o adenocarcinoma, com a maioria das lesões malignas ocorrendo em homens, com faixa etária de 60 a 69 anos. A imagem mais comum para casos de câncer foi lesão sólida maior que 8 mm com bordas irregulares encontradas no lobo superior do pulmão direito.

**Palavras-chave:** Neoplasias pulmonares; Epidemiologia; Histologia; Tomografia computadorizada por raios X; Neoplasias.

### Resumen

*Objetivo:* Describir y mejorar nuestra comprensión de la epidemiología del cáncer de pulmón. *Metodología:* Estudio epidemiológico retrospectivo, descriptivo y analítico, analizando tipo histológico, sexo, edad y resultados radiológicos para el cáncer de pulmón en la ciudad de Sinop - MT de 2014 a 2019. *Resultados:* Se analizaron 219 biopsias de lesiones. 113 (51,59%) confirmaron el diagnóstico de cáncer de pulmón. Los principales tipos histológicos para el diagnóstico histopatológico fueron el adenocarcinoma con un total de 47 (41,59%) casos, seguido del carcinoma de células escamosas con 27 (23,89%) casos. En cuanto al género, se encontraron 52 (46,02%) casos de cáncer de pulmón en mujeres y 61 (53,98%) casos en hombres. En general, el principal tipo histológico para ambos sexos fue el adenocarcinoma. En cuanto a la edad, el grupo etario predominante fue el de 60 a 69 años, con 43 casos (38,05%). En cuanto a las características de la imagen tomográfica para los casos de cáncer de pulmón, la localización del nódulo fue estadísticamente significativa, principalmente en el lóbulo superior del pulmón derecho, hallazgo observado en otras fuentes, donde el lóbulo superior derecho tuvo mayor incidencia de malignidad. *Conclusión:* el principal tipo histológico fue el adenocarcinoma, ocurriendo la mayoría de las lesiones malignas en hombres, con edades entre 60 y 69 años. La imagen más común para los casos de cáncer fue una lesión sólida mayor de 8 mm con bordes irregulares que se encuentra en el lóbulo superior del pulmón derecho.

**Palabras clave:** Neoplasias pulmonares; Epidemiología; Histología; Tomografía computarizada por rayos X; Neoplasias.

## 1. Introduction

Lung cancer is a commonly diagnosed, malignant lesion that presents the highest mortality rate for cancers worldwide (Araujo et al, 2018). In terms of histopathology, lung cancer is classified as: small-cell and large cell carcinoma, which include neuroendocrine carcinoma (include small cell carcinoma), adenocarcinoma, squamous cell carcinoma and large cell carcinomas (Husain, 2016).

Lung cancer is the third most common cancer in men in Brazil and the fourth most common in women. For each year of the triennial 2020-2022, there were an estimated 17,760 new lung cancer cases in men and 12,440 cases in women (Brasil, 2020).

In 70 to 95% of lung cancer cases, diagnosis occurs at an already advanced metastasized stage, leading to elevated mortality and consequently low survival, with only 18% of patients surviving more than 5 years (Araujo et al, 2018; Costa et al, 2020).

The majority of cases affect individuals between 50 and 70 years and although it was initially a disease that mostly affected men, lung cancer has become an increasingly common disease among women (Barros et al, 2006; Da Silva et al, 2021). In relation to sex, lung cancer incidence worldwide seems to be dropping in men following a peak, while rates have gone up among women (MacRosty & Rivera, 2020).

Notably, changes to the histopathological trends for lung cancer have been occurring in Brazil and around the world. Changes to smoking habits with the introduction of cigarettes with filters, have altered the epidemiology of lung cancer in developed nations, with an increased incidence of adenocarcinoma and a reduction in squamous cell carcinoma (Tsukazan et al, 2017; Alberg et al, 2005; Devessa et al, 2005; Charloux et al, 1997).

The little information available regarding histology, sex differences, age, radiological results and trends for lung cancer in the Brazilian population is mainly related to the Brazilian midwest. The present study seeks to describe and improve our understanding of lung cancer epidemiology, including its histology, sex distribution, patient age and radiological results for the disease.

## 2. Methodology

A descriptive and retrospective study (Serafim, 2009), analyzing tendencies over time, investigating data related to histological type, sex, age, and radiological results for lung cancer, through a review of biopsy results held at the Luigi Bogliolo Laboratory and imaging results held at the Sinop (MT) Center for Diagnostic Imaging during the period from 2014 to 2019.

In this manner, all diagnoses were collected from the same institution and analyzed by a single pathologist. The tomography images considered from the Diagnostic Imaging Center were also analyzed by a single radiologist.

The following variables were considered: age, sex and histological type, adenocarcinoma; squamous cell carcinoma; large cell carcinoma; neuroendocrine carcinoma; metastatic tumor; and carcinoid tumor/neuroendocrine tumor. Tomography variables included: size; location; border; necrosis presence; ground-glass presence; invasion of structures; atelectasis presence; lymphadenopathy presence; limits; damage to lobes; and number of nodules.

Microsoft Office Excel (version 2013) was used to tabulate the data, where the calculations related to descriptive statistics were realized, determining the absolute and relative frequencies.

The chi-square test was used to determine statistically significant associations ( $p \leq 0.05$ ), between neoplasm type and gender, age range and diagnostic year. Age brackets were divided from 30-39 years, 40-49 years, 50-59 years, 60-69 years, 70-79 years and  $> 80$  years. The same test was used to analyze the statistically significant relationship between neoplasm type and radiological findings. R Studio software was used for statistical analyses.

This research was approved by the Ethics Committee for Research with Human Beings/Sinop University Campus in the regular meeting on 13/09/2019 under Review Number: 3.573.362.

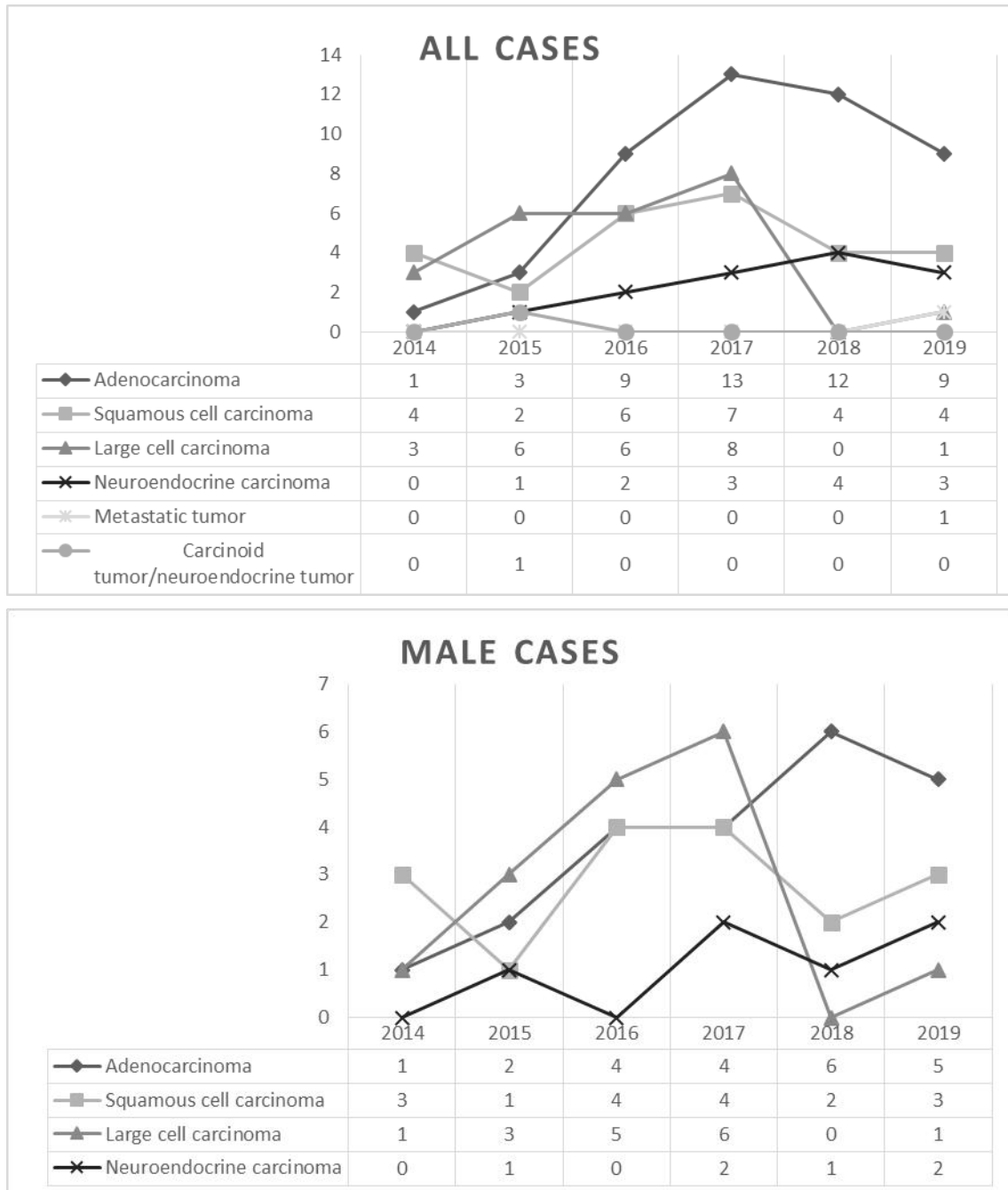
## 3. Results

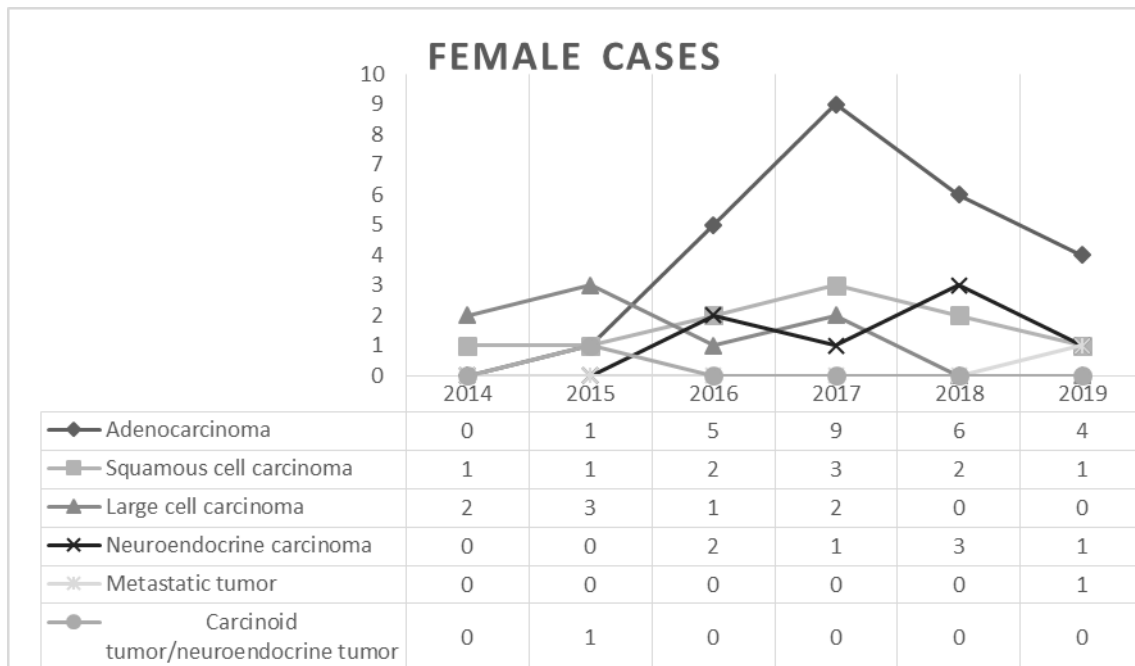
During the period from 2014 to 2019, 219 biopsies were performed on lesions suspected for lung cancer. A lung cancer diagnosis was confirmed in 113 (51.59%) of these. For histopathological diagnosis, the most common histological type was adenocarcinoma, totaling 47 (41.59%) cases, followed by 27 (23.89%) cases of squamous cell carcinoma, 24 (21.24%) other large cell carcinoma, 13 (11.50%) neuroendocrine carcinoma, one (0.88%) metastatic carcinoma and one (0.88%) carcinoid tumor/neuroendocrine tumor.

Analyzed by year, the greatest number of malignant lung lesions was observed in 2017, totaling 31 (27.43%) cases. A change in the histopathology subtype was also observed starting from 2016, when adenocarcinoma became the main type. Moreover, the squamous cell carcinoma subtype presented a reduction in numbers starting from 2017 onward. However, the histological type did not change significantly from 2014 to 2019 ( $p = 0.08$ ). One carcinoid tumor/neuroendocrine tumor was observed in 2015 and one metastatic carcinoma in 2019. (Figure 1.A).

In relation to sex, 52 (46.02%) lung cancer cases occurred in women and 61 (53.98%) in men. In total numbers, the main histological type for both sexes was adenocarcinoma, with a predominance in women with 25 (48.08%) cases to 22 (36.06%) cases in men, followed by squamous cell carcinoma with 17 (27.87%) cases in men and 10 (19.23%) cases in women. Analyzed by year, adenocarcinoma became the main histological type in women in 2016 and in 2018 for men, without a statistical difference between sexes or histological type ( $p=0.29$ ). (Figure 1.B and 1.C)

**Figure 1** - Histological type distribution for lung cancer in Sinop – MT between 2014-2019. A) All cases B) Male cases C) Female cases.





Source: Author himself.

Regarding age, the main age range was from 60-69 years, totaling 43 cases (38.05%), with 30 (69.77%) being men and 13 (30.23%) women. This was followed by the range from 50-59 years with 31 cases (27.43%) and afterward from 70-79 years with 26 cases (23.00%). Women were predominant in the age ranges younger than 60 years, while men predominated in the age range from 60-69 years and older than 80 years, without statistical difference between sexes for age ( $p=0.08$ ). (Table 1).

**Table 1** - Distribution by age range for lung cancer cases in Sinop – MT during the period from 2014-2019.

Variable	Lung cancer n (%)			p
Age range	Total	Men	Women	0.08
30-39 years	4 (3.54%)	1 (25.00%)	3 (75.00%)	
40-49 years	5 (4.42%)	2 (40.00%)	3 (60.00%)	
50-59 years	31 (27.43%)	13 (41.93%)	18 (58.07%)	
60-69 years	43 (38.05%)	30 (69.77%)	13 (30.23%)	
70-79 years	26 (23.00%)	12 (46.15%)	14 (53.85%)	
>80 years	4 (3.54%)	3 (75.00%)	1 (25.00%)	
<b>TOTAL</b>	<b>113</b>	<b>61</b>	<b>52</b>	

Source: Author himself.

Another observation from the study involved tomography imaging characteristics for lung cancer cases. It was not possible to access all the tomography images for the biopsies analyzed, but among those available ( $n=55$ ), the majority presented a solid lesion larger than 8 mm, in the right lung (32; 58.18%), with an irregular border (25; 45.45%), with absence of necrosis (42; 76.36%) and ground-glass (39; 70.91%), with the majority presenting invasion of structures (39; 70.91%), atelectasis (35; 63.64%), lymphadenopathy (28; 50.91%), undefined limits (32; 58.18%), damage to multiple lobes (29;

52.73%) and a single nodule (29; 52.73%) overall (Table 2). Demonstrating a statistically significant association in terms of the lesion location ( $p < 0.01$ ).

**Table 2** - Tomography characteristics for lung cancer cases in Sinop – MT during the period from 2014-2019.

Variables	n	%	p*
<b>Size</b>			0.91
Solid > 8 mm	54	98.18%	
Ground-glass > 8 mm	1	1.82%	
<b>Location</b>			<0.01
RL S I	4	7.27%	
RL S II	7	12.73%	
RL S IV	4	7.27%	
RL S V	2	3.64%	
RL S VI	6	10.91%	
RL S VII	1	1.82%	
RL S VII + VIII	1	1.82%	
RL S IX	4	7.27%	
RL S X	2	3.64%	
RL TOTAL	1	1.82%	
LL S I + II	9	16.36%	
LL S III	4	7.27%	
LL S VI	7	12.73%	
LL S VII	1	1.82%	
LL S IX	1	1.82%	
LL S X	1	1.82%	
<b>Border</b>			0.83
Spiky	4	7.27%	
Irregular + Spiky	13	23.64%	
Regular	13	23.64%	
Irregular	25	45.45%	
<b>Necrosis</b>			0.83
Present	13	23.64%	
Absent	42	76.36%	
<b>Ground-glass</b>			0.44
Present	16	29.09%	
Absent	39	70.91%	
<b>Invasion of Structures</b>			0.49
Present	39	70.91%	
Absent	16	29.09%	
<b>Atelectasis</b>			0.15
Present	35	63.64%	
Absent	20	36.36%	
<b>Lymphadenopathy</b>			0.15
Present	28	50.91%	
Absent	27	49.09%	

<b>Limits</b>			0.64
Defined	23	41.82%	
Undefined	32	58.18%	
<b>Damage to lobes</b>			0.44
Single	26	47.27%	
Multiple	29	52.73%	
<b>Number of nodules</b>			0.79
Single	29	52.73%	
Multiple	26	47.27%	

\*Chi-square Test. Legend: RL: right lung; LL: left lung; S: segment. Source: Author himself.

#### 4. Discussion

According to the most recent data published by the National Cancer Institute (INCA), lung cancer remains the most common cancer worldwide, occupying first place for men and third place for women (Brasil, 2020). Despite lung cancer being more prevalent in men, a finding that was also observed in this study, a tendency towards reduced rates of this cancer in men, contrary to what is observed in women with a tendency toward growing case numbers, reflects patterns of starting and quitting smoking (Brasil, 2020; Lortet-Tieulent et al, 2015). Specific data from GLOBOCAN 2012 regarding lung cancer incidence in 38 countries, showed that rates in men increased in 1 country, dropped in 22 and remained stable in 15 countries. For women, rates increased in 19 countries, dropped in 1 and remained stable in 18 countries (Bray et al, 2018). This could be related to the fact that, in historical terms, women started smoking later than men, in addition to lung cancer in nonsmokers being more common in women (Tsukazan et al, 2017; Patel, 2005).

History of smoking and age remain the main risk factors for developing cancer. Lung cancer is more common in men and women 70 years or older. These 70 years or older corresponded to 26.54% of cases in this study. Lung cancer has become the most common cause of death from cancer in men 40 years or older, which corresponds to 98.36% of cases in this study and in women with 60 years or older, corresponding to 53.85% of cases in this study (Bade & Cela Cruz, 2020; Siegel et al, 2019). Additionally, a study identified higher rates of lung cancer in young white women between 30 and 49 years, a finding that was observed in this study, wherein cancer in younger patients predominated in women (Jemal et al, 2018). Findings that corroborate traditional perspectives about lung cancer are changing.

A study limitation was the inability to identify if the patients who underwent a biopsy were smokers, information that was not presented in their medical records. However, it is known that smoking is the most important risk factor for lung cancer. An estimated 80 to 90% of lung cancers occur in smokers, with relative risk of carcinoma in smokers being 20 to 30 times higher than people who have never smoked (Wolpaw, 1996; Tyczynski et al, 2003; Alberg & Samet, 2003).

A change in histological epidemiology has been observed over recent years, with increased rates of adenocarcinoma and a reduction in squamous cell carcinoma. It is believed that the reduction observed in squamous cell carcinoma rates in Brazil is due to a reduction in the number of smokers since 1960, given the well demonstrated connection between this histological type and smoking. In addition to the advent of cigarettes with filters, which influences the smoker to prolong inhalation times to compensate for the lower quantity of smoke which passes through the filter, also leading to greater carcinogen deposits on the lung periphery, the most common location for adenocarcinomas (Tsukazan et al, 2017). Moreover, the chemical composition of new cigarettes with lower nicotine and tar levels, has an elevated quantity of nitrosamines. This is an important carcinogen related to adenocarcinoma, to the detriment of polycyclic aromatic hydrocarbons, another important carcinogen, but related to squamous cell carcinoma (Serafim, 2009). The present study already observed this histological change in Sinop, with adenocarcinoma being the predominant histological type for both sexes.

Computerized tomography (CT) provided data such as location, size, tumor volume, invasion of adjacent structures and metastases (de Souza, 2022). The development of imaging methods, especially from CT, has contributed enormously to the more precise location of pulmonary lesions (Chojniak et al, 2011). Furthermore, some characteristics of the image shown on the CT are suggestive of malignancy, such as: lesions with irregular or spiky borders, that account for 76.36% of the study sample. These are nodules with mixed attenuation, containing a solid component and a less dense component of ground-glass. The majority of lesions in the study were solid lesions, however 29.09% of the sample presented ground-glass in the image. Multiple nodules were observed in 47.28% of cases in this study (Gould et al, 2013; Kikano et al, 2015; Cardoso & Souza Júnior, 2014).

In terms of size, 100% of the lesions observed in the present study were larger than 8 mm. Risk of malignancy increases the larger the nodule size (maximum diameter). Images with less than 5 mm have a malignancy risk lower than 1% and do not require radiological monitoring according to the literature (da Rocha Leal, 2016). By comparison, nearly 80% of nodules larger than 20mm are malignant (Kikano et al, 2015).

The risk of malignancy is also greater with lesions of the upper lobes. There is an increased risk of malignancy in relation to the upper lobe with an odds ratio of 1.9. More specifically, the right upper lobe shows a greater rate of malignancy. This can be explained due to an increased flow of air into the upper right lobe during initial inspiration, and therefore, greater exposure to inhaled carcinogens, mainly in smokers. It is also possible for toxins and carcinogens to remain longer in the upper lobes due to lower efficiency of lymphatic elimination (Cruickshank et al, 2019; McWilliams et al, 2013; Horeweg et al, 2013; Jamnik et al, 2006). A statistically relevant finding from this study was that the majority of lesions observed were in pulmonary segments related to the upper right lobe. Segments I and II of the right lung correspond to the upper lobe, in which 20% of lesions were found.

## 5. Final Considerations

This study presents the current scenario for lung cancer in the Brazilian midwest. The fact that specific data and epidemiological work are frequently scarce or absent in Brazil should drive efforts to investigate this issue. Documenting epidemiological data is important, since it can inform public policy that provides preventative measures and early detection, seeking to reduce morbimortality rates and public expenditure.

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