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THYROID CANCER AMONG ANESTHESIOLOGISTS IN THE CITY OF MANAUS: INCIDENCE, DISEASE AND QUALITY OF LIFE FACTORS

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ABSTRACT

Objective: To investigate the incidence of thyroid cancer in anesthesiologists in the city of Manaus-AM, located in the Western Amazon, factors of illness and quality of life after treatment to which they were submitted. **Methods:** Observational, analytical, cross-sectional study, approved by the Research Ethics Committee of the Fundação Centro de Oncologia do Amazonas. Data collection was performed using an instrument built by the research team and through the University of Washington's Quality of Life Assessment Questionnaire (UW-QoL). Descriptive and exploratory analysis of the data was carried out and the results were expressed in tables and figures. Relationships between variables were verified using Pearson's Chi-Square test and ANOVA and the correlations between variables by Spearman's correlation coefficient. **Results:** 22 anesthesiologists showed changes in the thyroid, and in 12 (54.54%) professionals the changes were benign or malignant neoplasms; only age group was related to the occurrence of neoplasia and as for quality of life, the variable with the lowest score was appearance. **Conclusion:** Incidence of thyroid neoplasia presented in this study, greater than in any other group of health professionals, it may suggest the need for screening for thyroid changes through ultrasonography in these professionals.

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INTRODUCTION

Thyroid cancer is the most common malignant neoplasm of the endocrine system and its incidence has increased globally faster than that reported for other solid tumors in recent decades (Wiltshire *et al.,* 2016; Vaccarella, 2016). According to the World Cancer Report 2020 (Wild *et al.,* 2020), over the past three decades, the incidence of thyroid cancer in adults has doubled, tripled, or even more in several high Human Development Index (HDI) countries, and may become the fourth most common cancer by 2030 in the United States of America (USA) (Rahib *et al.,* 2014). In 2018 there were 567,000 new cases, equivalent to 3% of all estimated cancers occupying the ninth position in the world with 436,000 new cases in females (11.5 per 100,000) and 131,000 male cases (3.4 per 100,000) (Bray *et al.,* 2018; Ferlay *et al.,* 2019) with the highest incidence rates being seen in North America, mainly in Canada, Australia and New Zealand, and in East Asia, mainly in South Korea and Polynesia. Sharp increases have also been seen in middle-income countries such as Brazil, China, and Turkey [3]. According to data corroborated by the National Cancer Institute José Alencar Gomes da Silva (INCA) (Ministério da Saúde, 2020), it is estimated, in particular for Brazil that, for each year of the triennium 2020-2022, 1,830 new cases in men and 11,950 in women. These values correspond to an estimated risk of 1.72 new cases per 100,000 in men and 11.15 per 100,000 in women and, excluding non-melanoma skin tumours, thyroid cancer also occupies the ninth position in the northern region of Brazil (2.84/100,000), and the state´s capital, Manaus accounting for the estimate for 2020 of 50 new cases in women and less than 20 cases in men, totalizing 350 cases in the entire territory of the State of Amazonas (Ministério da Saúde, 2020). Although the precise causes of thyroid cancer remain uncertain, some risk factors, such as radiation exposure, sex (women)

and a low iodine diet (are known to increase the risk of follicular thyroid cancer) (American Society Cancer, 2020; American Cancer Society, 2015) as well as an iodine-rich diet (may also increase the risk of papillary-type cancer) [8] have been consolidated. Genetic conditions have been also associated with different types of thyroid cancer, being the highest rates among people with familial adenomatous polyposis, Gardner syndrome, Cowden disease, and Carney complex type I (American Society Cancer, 2020). Recently, several lifestyle factors have been suggested to be associated with the risk of developing thyroid cancer from the results of observational studies. In 2012, Zhao and colleagues (Zhao *et al.,* 2020), reported that overweight and obesity increased significantly the risk of thyroid cancer (by 18%) from the results of a meta-analysis of seven cohort studies. Similarly, in 2019, through a nationwide population-based cohort study involving 11,323,006 adults, Kwon and colleagues (Kwon *et al.,* 2019), demonstrated that higher body mass index and higher abdominal circunference, were significantly associated with an increased risk of thyroid cancer and that weight gain in lean individuals were associated with an increased risk of thyroid cancer, and weight reduction in individuals with obesity was associated with a decreased risk of thyroid cancer as well.

Furthermore, epidemiological studies on occupations and occupational exposures and the incidence of thyroid cancer have been described with emphasis on the category of diagnostic and treatment health professionals, including dentists, maxillofacial surgeons, pharmacists, physical therapists, health technologists and technicians, nurses, surgeons, and anesthesiologists. Ashbrook-Kilfoy and colleagues (Aschebrook-Kilfoy, 2011), 2014, examined this incidence of thyroid cancer among occupations or occupational exposure and found that the most consistent associations were in workers exposed to radiation and occupations in health services. Similarly, Kitahara and colleagues (2018) in a study that included 89,897 radiology technologists in the United States, where 476 cases of thyroid cancer were identified, found that the incidence of thyroid cancer was 1.61 times higher than that of the general population. Regarding physicians, because they are part of a unique group of individuals who are routinely exposed to carcinogens such as ionizing radiation on and various chemicals, Zielinski and colleagues (2014) in a Canadian National Registry cohort study of 67,562 medical workers (23,580 men and 43.982 women), exposed to ionizing radiation, confirmed an increased risk of thyroid cancer among physicians occupationally exposed to ionizing radiation, and although Lee and colleagues (2019), found no significant evidence that thyroid cancer incidence rates among Korean medical radiologists were associated with occupational radiation dose, these professionals also had slightly higher thyroid cancer incidence rates than the general population.

With the rapid development of new interventional techniques in cardiology, radiology, gastroenterology, neurosurgery, pneumology, and other areas, the responsibilities of the anesthesiologist are no longer limited to providing care in traditional operating rooms. Now, it includes computed tomography, nuclear medicine procedures, interventional radiology, cardiac catheterization and electrophysiology procedures, causing more ionizing radiation exposure to this professionals (Phillips, 2011; Boggs *et al.,* 2017). Moreover, taking the USA as an example, every year approximately 50 million general anesthesia are performed (Ishizawa, 2011), in which the great majority of them use halogenated inhalation agents, including sevoflurane, desflurane, isoflurane, and non-halogenated agents such as nitrous oxide. In this context, a small fraction of these inhaled anesthetics is metabolized in the patient's body and the rest is eliminated in the operating room. This residual anesthetic gas are bioaccumulative and have toxic chemicals that degrade slowly, promoting cumulative adverse effects in the short and long term (Ishizawa, 2011; Jain *et al.,* 2019). Studies have shown that this long-term exposure can lead to increased oxidative stress (Baysal *et al.,* 2009; Wronska-Nofer *et al.,* 2009), DNA damage[22], and carcinogenesis (Sivaci *et al.,* 2006). Although thyroid cancer has a good prognosis and high survival rates, the diagnosis of cancer remains difficult to accept and because of that has a significant impact on the quality of life of these patients transforming a healthy status in a cancerous subject (Haraj, 2018). In this scenario, important questions arise, such as: what would be the incidence of thyroid cancer in these professionals and also,how the consequences of this type of cancer would affect the quality of life of those patients, being in along, aggressive and sometimes mutilating treatmentthat consequently interfere with daily activities, concerning to functionality and self-image of the affected individual (Haraj, 2018). Therefore, the objective of this study was to determine the incidence of thyroid cancer among anesthesiology physicians in the city of Manaus, Brazil and the factors that may be associated with it. This investigation was also aimed to recognize the quality of life of these professionals after the treatment they underwent.

MATERIAL AND METHODS

Ethical aspects: This study was submitted to the PlataformaBrasil, a system linked to the Research Ethics Commission - CONEP and Research Ethics Committee (CEP), approved on March 9, 2020, CAAE: 24528619.5.0000.0004, Opinion number: 3.905.470.

Study design: An observational analytical, cross-sectional study whose study population was a group of anesthesiology physicians who work in the city of Manaus - AM, located in Western Amazon, Brazil. Informed consent was obtained from all participants, and those who presented neurological or cognitive deficits were excluded. The eligibility criterion was to have thyroid disease or to have undergone thyroidectomy.

Sample size: The sample size was estimated as the total number of anesthesiology physicians working in the city of Manaus, 200 professionals total, and by the prevalence of professionals affected by thyroid cancer, found in a study by Lu et al. (2014), which was 1.10%. We determined a precision (margin of error) of 4.0% and a confidence level of 95%, which resulted in a sample size of 22 anesthesiologists.

Research procedure: After prior information about the objectives of the research, the professionals who met the inclusion criteria were invited to answer the questionnaires related to it. In this study, two data collection instruments were used, called Instrument 1 and Instrument 2. Instrument 1consisted of exploratory data with variables related to the anesthesiologists' lifestyle and clinical characterization of the disease, which involved information about its characteristics andchoosen treatment. This instrument was created by our research team and validated by peers (head and neck specialists in epidemiology and collective health areas), whoobtain information about the origin of the study participants, some general social conditions (age, gender, height and weight, marital status, religion, education, and occupation), predisposition to the disease and exposure to risk factors (work environment - private clinic versus university hospital - how many years in working as an anesthesiologist when diagnosed, theworkload at the time of cancer diagnosis, history of the disease, past surgical history and results of health exams, care history (conditions of diagnosis and treatment - what type of cancer and how it was diagnosed). Instrument 2 consisted of a University of Washington Quality of Life Assessment Questionnaire (UW-QoL) - validated for the Brazilian population, which is specific for evaluating patients with head and neck cancer. This instrument contains 12 questions (or domains) related to head and neck, activity, recreation, pain, mood, and anxiety. Each question has three to five answer categories, with scores ranging from zero (worst score) to 100 (best score).

Statistical analysis: The variables were tabulated and analyzed using the IBM SPSS Statistics version 21 statistical program, with a descriptive, exploratory and inferential analysis of the data and the results were presented in frequency tables and graphs. The domains of quality of life were found in accordance with the standards of the Quality of Life instrument of the University of Washington (UW-QoL) and the relationships among domains as well as the most relevant variables were verified through the Analysis of Variance or

ANOVA of Kruskal-Wallis, considering the 5% level of statistical significance.

RESULTS

General characterization of the sample: The sample consisted of 22 anesthesiologists working in the city of Manaus, most of them being female 90.9% (20), white 63.6% (14), married 72.7% (16). Concerning to academic education, 16 had specialized in Manaus, 3 in Rio de Janeiro, 2 in São Paulo and 1 in Brasília. The mean age (years) of these professionals was 47.27, weight (Kg) 72.64, BMI 27.17 and time of professional activity at the time of data collection (years) was 18.41 (Table 1). Regarding risk factors, 22 participants reported exposure to ionizing radiation in the work environment, 14 had afamily history of cancer, 4 used alcohol and 1 reported smoking; as for anesthetic practice, 13 performed balanced general anesthesia (intravenous+inhalation) in their daily routine, 6 performed neuroaxial block, and 3 performed total intravenous anesthesia (Table 2).

Table 1. Descriptive analysis of personal characteristics: age, weight, height, BMI, time since graduation, and of the anesthesiologists in the research. Manaus, Amazonas, Brazil, 2020

CHARACTERISTICS	n	DESCRIPTIVE MEASURES					
		Average	dp[1]	Lowest	Median	Maximum	IQR[2]
Age	22	47,27	8,42	31,00	48,00	67,00	13,00
Weight	22	72,64	13,43	46,00	72,50	100,00	21,50
Height	22	1,64	0,08	1,52	1,63	1,85	0,10
BMI	22	27,01	4,97	18,43	25,84	36,72	6,11
Graduation Time	22	17,68	8,75	3,00	19,00	37,00	12,00

[1]dp= standard deviation; [2]IQR = Interquartile range

Table 2. Risk factors investigated in the anesthesiologists evaluated. Manaus, Amazonas, Brazil, 2020

RISK FACTORS		n*	%
Exposure to radiation	Yes	22	100
	No	0	0
Most commonly used anestesia	Balanced (inhaled)	13	59,1
	Neuroaxial block	6	27,3
	General intravenous total	3	13,6
Etilism	Yes	4	18,2
	No	18	81,8
Tabagism	Yes	1	4,5
	No	21	95,5
Family history for cancer	Yes	14	63,6
	No	8	36,4
Had other neoplasia	Yes	1	4,5
	No	21	95,5
			*n=22

Table 3: Risk factors in anesthesiologists affected by thyroid cancer. Manaus, Amazonas, Brazil, 2020

RISK FACTORS		n*	%
Exposure to radiation	Yes	12	100
	No	0	0
Most commonly used anestesia	Balanced (inhaled)	6	50
	Neuroaxial block	5	41,7
	General intravenous total	1	8,3
Etilism	Yes	2	16,7
	No	10	83,3
Tabagism	Yes	1	8,3
	No	11	91,7
Family history for cancer*	Yes	7	58,3
	No	5	41,7
Had other neoplasia	Yes	1	8,3
	No	11	91,7
			*n=12

General characterization of the sample of anesthesiologists who presented thyroid neoplasia: Of the anesthesiologists affected by thyroid cancer, 11 (91.7%) were female, 10 (83.3%) were over 45 years old at the time of data collection and 2 (16.7%) under 44 years old. As for weight, 1 (8.3%) had type I obesity, 1 (8.3%) type II obesity, and 5 (41.7%) were overweight. 2 (16.7%) professionals were alcohol consumers and 1 (8.3%) smoker. In this sample, 7 (58.3%) had a family history of cancer and all reported exposure to ionizing radiation during anesthesia activity and in the work routine, 6 (50.0%) used mainly general anesthesia (balanced/inhaled) (Table 3). Regarding the time of diagnosis of neoplasia, 8 (66.7%) performed anesthesia between 1 and 10 years, 3 (25.0%) between 10 and 20 years, and 1 (8.3%) for more than 20 years ago. Regarding the treatment of the neoplasia, 10 (83.3%) underwent total thyroidectomy, 1 (8.3%) total thyroidectomy plus iodotherapy and 1 (8.3%) partial thyroidectomy andhistopathological results were 7 benign and 5 malignant (3 papillary, 1 micropapillary and 1 mixed tumor (Table 4).

Table 4. Clinical characteristics, treatment, and histological type of neoplasms in anesthesiaologists. Manaus, Amazonas, Brazil, 2020

CHARACTERISTICS		n*	%
Had thyroid neoplasm	(n=22)		
	Yes[1]	12	54,5
	No	10	45,5
How many years had you been in anesthesia (years)	01 a 10	8	66,7
	10 a 20	3	25,0
	> 20 years	1	8,3
Diagnostic method	Image	0	0,0
	Laboratory / Image	12	100,0
Treatment	Partial Thyroidectomy	1	8,3
	Total Thyroidectomy	10	83,3
	Total Thyroidectomy + iodotherapy	1	8,3
Histopathological type	Benign Nodules	5	41,7
	Benign Hyperplasia	1	8,3
	Benign goiter	1	8,3
	Micropapillifer	1	8,3
	Papillifer	3	25,0
	Mixed Tumor	1	8,3
Already had another neoplasm	Yes	1	8,3
	No	11	91,7
[1]All 12 had primary neoplasm			*n=12

Table 5. Correlation between the presence of thyroid neoplasia in anesthesiologists and socio-demographic characteristics and risk factors

CHARACTERISTICS	CORRELATION	*p* *
Gender	0,029	0,899
BMI classification	0,085	0,708
Color	0,356	0,104
Age range	-0,443	0,039*
Marital status	0,369	0,091
Children	0,239	0,284
Religion	0,043	0,849
Type of anestesia	-0,123	0,586
Tabagism	-0,043	0,849
Etilism	0,199	0,374
Family history	-0,121	0,592
* p values are significant for p ≤ 0,05 (5%)		
Spearman´s correlation coefficient		

Table 5 shows evidence that age was correlated to the occurrence of neoplasm in the evaluated anesthesiologists (p=0.039) and Table 6 shows the quality of life of anesthesiologists who underwent treatment for thyroid cancer; among the twelve domains of the UW-QoL questionnaire, the variable with the lowest score was appearance (975) and the highest scores were swallowing, saliva, and chewing (1,200).

Table 6. Analysis of Quality of Life of Anesthesiologists with thyroid neoplasm, according to the UW-QoL domains Manaus, Amazonas, Brazil, 2020

UW-QoL DOMAIN	n	DESCRIPTIVE MEASURES						
		ADD	Average	dp	Minimum	Average	Maximum	IQR
Pain	12,0	1050,0	87,5	13,1	75,0	87,5	100,0	25,0
Appearance	12,0	975,0	81,3	18,8	50,0	75,0	100,0	25,0
Activity	12,0	1050,0	87,5	13,1	75,0	87,5	100,0	25,0
Recreation	12,0	1050,0	87,5	16,9	50,0	100,0	100,0	25,0
Swallowing	12,0	1200,0	100,0	0,0	100,0	100,0	100,0	0,0
Chewing	12,0	1200,0	100,0	0,0	100,0	100,0	100,0	0,0
Speech	12,0	1167,0	97,3	9,5	67,0	100,0	100,0	0,0
Shoulder	12,0	1167,0	97,3	9,5	67,0	100,0	100,0	0,0
Taste	12,0	1167,0	97,3	9,5	67,0	100,0	100,0	0,0
Saline	12,0	1200,0	100,0	0,0	100,0	100,0	100,0	0,0
Humour	12,0	1150,0	95,8	9,7	75,0	100,0	100,0	0,0
Anxiety	12,0	1134,0	94,5	12,9	67,0	100,0	100,0	0,0
Total Media Score	**24,0**	**1125,8**	-	-	-	-	-	-
Average Combined Score	**24,0**	**93,8**	-	-	-	-	-	-

In our study, 22 anesthesiologists showed changes in the thyroid, and in 12 (54,54%) professionals the changes were neoplastic (benign or malignant) resulting in an incidence of 6%; considering data from the Association of Anesthesiologists of the State of Amazonas / ASSALAM 2019, which counted two hundred anesthesiologists as partners, 101 of which were female and 99 were male, In view of this, thyroid malignancy was 2.5%, an occurrence, above the incidence of 1.10% found by Lu and collaborators (Lu *et al.,* 2014) This research also pointed out in this medical population, 500 cases for every 100 thousand men and 5,500 for each 100 thousand women when it was considered benign and malignant neoplasia and a rate of 500 cases for every 100 thousand men and 2.000 for every 100 thousand womenwhen only malignancy was considered. The rates found in this research, unlike other studies (Bray *et al.,* 2018; Ferlay *et al.,* 2019; Ministério da Saúde, 2020), can be directed to that found by other authors (Aschebrook-Kilfoy *et al.,* 2014; Kitara *et al.,* 2018; Zielinski *et al.,* 2009), who observed an increase in the incidence of thyroid cancer among professionals who work with medical or diagnostic radiation and with findings of the analysis in South Korean radiation technologist workers in Lee's research (Lee *et al.,* 2019), because in our sample, apparently,the participants had more risk factors than exposure to ionizing radiation. Considering that, according to Volquind et al. (2013), work environments where anesthesiologists spend most of their time in their professional practice, they are unhealthy places due to the risks they can bring, because, in addition to exposure to ionizing radiation, there are also risks from anesthetic gases and vapors residuesincreasing the possibility of incidence of thyroid cancer. Among the 22 eligible participants for the study,10 were carriers of thyroid diseases, being, Hashimoto's thyroiditis (6), thyroid nodules being monitored (2), BasedowGraves disease (1), in an undiagnosed investigation (1); in contrast, the remaining members who underwent thyroidectomy for thyroid neoplasia, 7 had abenign result (nodules, hyperplasia, goiter, and five had malignancy (papillary, micropapillary, mixed tumor) confirmed by histopathology.

This scenario of benign thyroid diseases in ten doctors, calls attention to a pooled analysis of 14 case-control studies of thyroid cancer, 2,725 cases and 4,776 controls, where several factors were investigated and the strongest and most consistent results of this case-control analysis were about benign thyroid conditions, particularly goiter nodules/adenomas and hyperthyroidism[28], not the object of this study. In addition, some studies have shown an increased risk of thyroid cancer in patients with Hashimoto's thyroiditis (Lai *et al.,* 2017; Liu, 2017). Through descriptive analysis, some events were verified among the professionals who underwent treatment for thyroid cancer, already imputed in previous studies as factors of disease, as follows: a) exposure to ionizing radiation (Aschebrook-Kilfoy *et al.,* 2014; Kitara *et al.,* 2018; Zielinski *et al.,* 2009; Lee *et al.,* 2019), all participants in this study reported exposure both in the operating room environment and in the diagnostic and therapeutic nuclear medicine environment; b) female gender and age, according to several studies (Bray, 2018; Ferlay, 2019; Ministério da Saúde, 2020), thyroid cancer occurs more in women than men (11: 1 in this research) and most in reproductive age between 20 to 50 years with the incidence decreasing after menopause[31] and men usually between 60 and 70 years.Our results showed that eleven female members were between 20 to 50 years at the time of diagnosis; c) family history for cancer, some inherited conditions have been associated with different types of thyroid cancer as well as family history (American Society Cancer, 2020; Pinheiro, 2017), seven of the participants in this research had a family history for cancer, two of the family members were ever thyroid cancer. However, the adverse effects of anesthetic gas residues on themedical staff are still controversial and difficult to measure; studies have shown that exposure induces cumulative genotoxic effects[33] and is also an important factor in the increasing risk of DNA damage[22,34] and oxidative stress (Baysal *et al., 2009;* Wronska-Nofer, 2009; Costa Paes *et al.,* 2014). Some other factors (body mass index, colour smoking, alcohol consumption) were also visualized in this survey, but when Spearman's Correlation Coefficient was applied, there was evidence that only the age group was correlated to the occurrence of cancer in the anesthesiologists evaluated (p=0.039), which could mean that the older the professional, the greater the probability of the occurrence of the disease. As for thequality of life (QoL), among the twelve domains of the UW-QoL questionnaire, the variable that presented the lowest score was appearance (975), which is in agreement with the Choi[35] study where post-thyroidectomy scars on the neck affected the QoL of patients with thyroid cancer, regardless of the type of scar; however, complications of the treatment such as hypocalcemia, vocal cord paralysis caused by total thyroidectomy and the occurrence of second cancer caused by radiotherapy were not observed in this study.

CONCLUSION

This research showed an incidence of thyroid cancer in a group of professionals, who are not normally subject to surveillance, greater than in any other group of health professionals, and, since anesthesiologists are subjected to a series of occupational risks due to the workplace and professional activity, such as toxicity of anesthetic gases, exposure to ionizing radiation, among others andilness factors that are more difficult to be predicted and measured, it is suggested to continue this study, including with larger sampling, a limiting factor of this study, and also screening for thyroid through ultrasonography in these professionals.

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