ramr
American Review of Respiratory Medicine
Revista Americana de Medicina Respiratoria

ORIGINAL ARTICLE

ISSN 1852-236X

Prevalence of Thoracic Metastases in Patients with Thyroid Cancer at the National Cancer Institute between 2016 and 2019 in Bogotá, Colombia

Prevalencia de Metástasis torácicas en pacientes con cáncer de Tiroides en el Instituto Nacional de Cancerología entre 2016 y 2019, en Bogotá, Colombia

Estévez-Ramírez, Gloria M.[1,2]; Mejía-Sandoval, Harvey J.[3]; Saavedra, Alfredo[4]; Callejas, Ana Milena[4]; Sánchez-Morales, Edgar A.[4]

Received: 11/25/2022
Accepted: 08/16/2023

Correspondence
Gloria Estévez-Ramírez.
E-mail: gestevezr@unal.edu.co

ABSTRACT

Introduction: Thyroid cancer is the most prevalent endocrine neoplasm and the third most common tumor in Colombian women. It has a good prognosis in the absence of metastasis. The lungs are the most affected tissue by metastasis in patients with thyroid cancer. The objective of this work was to describe the prevalence of thoracic metastases in patients with thyroid cancer in a cancer reference hospital from Bogotá, between 2016 and 2019.

Materials and methods: The study was cross-sectional, with non-probabilistic sampling of consecutive cases in patients older than 18 with thyroid cancer who were attended at the National Cancer Institute between 2016 and 2019.

Results: 241 patients were included in the study; 53 had thoracic metastases. The mean age of patients with metastasis was 59.6 years (SD ± 12.7); 77.3% were female and 90.5% showed papillary carcinoma. The prevalence of thoracic metastases was 21.9%. The most common comorbidity was arterial hypertension (32.08%). The most common symptom was dyspnea, with 15%. 34% of patients had thyroglobulin of more than 38 ng/ml and 22% had detectable anti-thyroglobulin antibodies.

Variables associated with thoracic metastases were age ($p = 0.002$), weight ($p = 0.019$), cervical adenopathies ($p = 0.007$), presence of dyspnea ($p = 0.004$), and thyroglobulin values greater than 38 ng/ml ($p < 0.001$). Cervical adenopathies were found in 86% of patients with metastasis, suggesting the fact that they are a risk marker for metastasis.

Conclusions: This study allows us to establish local data, whose results promote future prospective studies that identify associated variables and prognostic factors in patients with thyroid cancer.

Key words: Thyroid neoplasms; Metastasis, Prevalence

Rev Am Med Resp 2023;23:161-167
https://doi.org/10.56538/ramr.NMDQ1943

[1] Fellow of Pneumology Universidad de la Sabana
[2] Internist physician Universidad Nacional de Colombia
[3] Endocrinologist Universidad Nacional de Colombia
[4] Pulmonologist Universidad Nacional de Colombia - Instituto Nacional de cancerología

RESUMEN

Introducción: El cáncer de tiroides es la neoplasia endocrina más prevalente y el tercer tumor más frecuente en las mujeres colombianas. Tiene buen pronóstico en ausencia de metástasis. Los pulmones son el tejido más comprometido por metástasis en pacientes con cáncer de tiroides. El objetivo del trabajo fue describir la prevalencia de las metástasis torácicas en pacientes con cáncer de tiroides en un centro de referencia en cáncer de la ciudad de Bogotá entre 2016 y 2019.

Material y métodos: El estudio fue de corte transversal con muestreo no probabilístico de casos consecutivos en pacientes mayores de 18 años con cáncer de tiroides que asistieron a consulta externa de del Instituto Nacional de Cancerología entre 2016 y 2019.

Resultados: Se incluyeron 241 pacientes; 53 presentaron metástasis torácicas. Dentro de los pacientes con metástasis el promedio de edad fue de 59,6 años (DE ± 12,7), 77,3% fueron mujeres, y el 90,5% presentó carcinoma papilar. La prevalencia de metástasis torácicas fue del 21,9%. Las comorbilidades más frecuentes fueron hipertensión arterial (32,08%). El síntoma más frecuente fue la disnea en un 15%. El 34% presentaron tiroglobulina mayor de 38 ng/mL y un 22% tenían anticuerpos antitiroglobulina detectables. Las variables asociadas a metástasis torácicas fueron la edad (p = 0,002), el peso (p = 0,019), adenopatías cervicales (p = 0,007), presencia de disnea (p = 0,004) y tiroglobulina mayor de 38 ng/mL (p < 0,001). La presencia de adenopatías cervicales se encontró en el 86% de los pacientes con metástasis, lo que sugiere que se trata de un marcador de riesgo de metástasis.

Conclusiones: El presente estudio permite establecer datos locales, cuyos resultados promueven futuros estudios prospectivos que identifiquen variables asociadas y factores pronósticos en pacientes con cáncer de tiroides.

Palabras clave: Neoplasias de la tiroides; Metástasis; Prevalencia

INTRODUCTION

Thyroid carcinoma is the most common endocrine neoplasm;[1] it has a low incidence, and it predominantly affects the female population.[2] In Colombia, it is the third most frequent neoplasm in women[3]. Usually, it follows a benign clinical course, especially when the histological type corresponds to differentiated carcinoma (papillary and follicular carcinoma) and it has 10-year survival rates that exceed 90%.[3] However, the presence of metastasis leads to a decreased life expectancy and a worse clinical course of the disease.[4]

When there is metastatic involvement, the lungs are the most commonly affected organs. The prevalence of lung metastasis from thyroid carcinoma varies in different cohorts and ranges from 2% to 20%.[5-7] Asian studies have characterized lung metastases in patients with thyroid carcinoma. However, in clinical practice, it is observed that not only pulmonary involvement occurs; there is also mediastinal, pleural, intrathoracic airway, and chest wall involvement.[8,9]

The purpose of this study was to determine the prevalence of thoracic metastases (lung, mediastinal, pleural, intrathoracic airway, and chest wall) in patients with thyroid carcinoma, and to describe the sociodemographic, histopathological, clinical, and exposure-related characteristics of patients affected by thoracic metastases.

MATERIALS AND METHODS

An observational, cross-sectional period study was conducted with retrospective data collection. The data were extracted from the clinical records system of the National Cancer Institute (INC). A sample size of 219 patients was calculated, aiming for 95% power and a 5% alpha error. Accounting for potential losses of 10%, a final sample size of 241 patients was determined. The study included patients with a confirmed diagnosis of thyroid carcinoma, including all histological subtypes, who attended the outpatient service between January 1, 2016, and December 31, 2019, in Bogotá, Colombia. Individuals under 18 years of age, pregnant women, and cases with more than 30% missing required data were excluded.

The independent variables encompassed sociodemographic factors, comorbidities, previous exposures, treatment, thyroglobulin levels, anti-thyroglobulin antibodies, and the primary dependent variable: the presence of thoracic me-

tastases. Data collection was carried out using the Research Electronic Data Capture (REDCap) platform at the NCI.

A descriptive analysis was performed, using measures of central tendency and dispersion (mean and standard deviation, or median and interquartile ranges), depending on the distribution of quantitative variables. Qualitative variables were expressed as absolute and relative frequencies. Subsequently, a group comparison analysis was conducted using statistical tests such as the Chi-square test or Fisher's exact test, based on the available data in each category for the collected variables, mostly focusing on qualitative variables. Finally, a bivariate logistic regression was conducted for the association analysis. The database was analyzed using Stata 15.0 software.

Ethical considerations were duly observed for the execution of this project, following both national and international guidelines for clinical research involving human subjects. The researchers were trained and certified in good clinical practices, and the project received approval from the medical ethics committees of the Universidad Nacional de Colombia and the National Cancer Institute.

RESULTS

Between January 2016 and December 2019, 241 patients met the inclusion criteria. The primary outcome, the prevalence of thoracic metastasis, was 21.9%. The identification of the prevalence of each type of thoracic metastasis showed the following results: 19% for lung metastasis, 0.41% for pleural metastasis, 0.83% for mediastinal metastasis, 0.83% for airway metastasis, and 0.83% for chest wall metastasis.

Among the total patients with thoracic metastasis, 86.79% of the cases were lung metastasis, 3.77% mediastinal metastasis, 1.9% pleural metastasis, 3.77% had chest wall involvement, and in 3.77% of the cases, the airways were affected (Figure 1).

77.35% of patients with thoracic metastasis were female. The mean age of patients with metastasis was 59.6 years (SD +14.3). 71.7% of patients were older than 55 years.

Regarding the histological type, 90.57% had papillary cancer, 1.89% had follicular cancer, 1.89% medullary cancer, 1.89% anaplastic cancer, and 3.78% showed two histological types (follicular and papillary, or follicular and medullary).

67.9% of patients with metastasis showed stages I and II (annexes 1 and 2). The most common comorbidities were arterial hypertension (32.08%) and kidney disease (7.5%). 5.6% had associated lung disease, and 9.43% and 1.89% had a history of active smoking and radiation exposure, respectively. 86% had concomitant involvement of cervi-

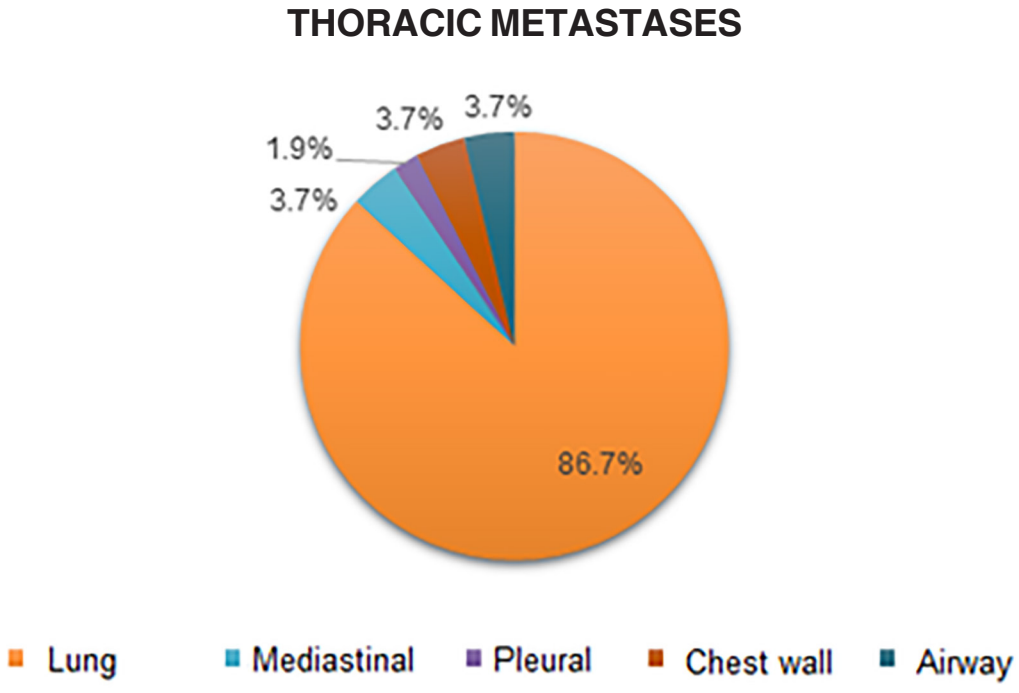

Figure 1. Frequency distribution of thoracic metastases

cal lymph nodes. In terms of the treatments that were administered, 96.2% underwent total thyroidectomy, 86.7% lymph node dissection, 77.3% had initial iodine therapy, and 24.53% required additional doses of radioactive iodine as part of metastasis management. 11.32% of patients were managed with tyrosine kinase inhibitors.

Regarding the symptoms, 15.09% presented with dyspnea, and 9.43% had cough.

When evaluating laboratory results, it was observed that 34% of patients with metastasis had a thyroglobulin level above 38 ng/ml, which was different from patients without metastasis, where such thyroglobulin values (above 38 ng/ml) were found in 2.7%. 22% of patients with thoracic metastasis had detectable anti-thyroglobulin antibodies.

When comparing patients with thoracic metastasis with those without metastatic involvement, a statistically significant difference was found in variables such as: age (p=0.0022), clinical stage (p = <0.001), BMI (p=0.027), kidney disease (p = 0.022), cervical lymph node involvement (p = 0.003), active smoking (p=0.027), presence of dyspnea (p=<0.001), and thyroglobulin above 38 ng/ml (p = <0.001).

Table 1 summarizes the characteristics of the sample in general, as well as the characteristics of the group with thoracic metastasis and the group without metastatic involvement.

In the bivariate analysis, a higher prevalence of thoracic metastasis was observed in patients over 55 years of age, weighing less than 60 kg, with thyroglobulin levels above 38 ng/ml, and with involvement of cervical lymph nodes and dyspnea. Results are shown in Table 2.

DISCUSSION

This study allows determining local data regarding the prevalence of thoracic metastasis in thyroid cancer and the factors associated with the presence of thoracic metastasis. This information allows observing the frequency of this neoplasm when it shows metastatic involvement and identifying variables that could be related to the presence of metastasis. These would provide valuable information for future studies that contribute to the documentation of predictive factors for thoracic metastasis in the local population with thyroid cancer. These data have not been previously described.

The prevalence of thoracic metastasis at 21.9% differs from national and international data. Data provided by a study conducted in Manizales, Colombia, reported an overall prevalence of distant metastasis (both thoracic and extrathoracic) of 1% in men and 1.04% in women[10]. Regarding international data, the study of Chen et al. reported a prevalence of 10.19%[11]. The study by Song et al conducted in China, reported a prevalence of 7.95% for lung metastasis. These percentage differences in prevalence could be attributed to the fact that our population comes from a national cancer reference center.

Sociodemographic data in terms of gender distribution align with the globally reported predominance of involvement in women[2,12]. 77.35% of patients with metastasis were women, similar to the Asian cohorts of Sabra et al[13] and Liete et al[14], who reported that 53% and 64.8% of patients with metastasis were women, respectively. However, with regard to age, the mean age wasn't similar to other studies. In Brazil, a study conducted by Leiet et al[14] found that 68.5% of patients were over 45 years old. In Asian studies like that of Sabrá et al[13] and Chopra[15], patients with metastasis had a mean age of 52 and 45 years, respectively. This suggests that Latin American populations likely tend to exhibit thoracic and lung metastasis at a later stage compared to Asian populations. This finding could be explained by genetic characteristics unique to our population or by barriers of access to diagnostic methods within the system.

The distribution of histopathological types among patients with thoracic metastasis was similar to what is reported in the global literature[6,13], with a higher prevalence of papillary cancer. Regarding the stage at the time of diagnosis, in this study, 67.9% of patients with metastasis were in stages I and II at the time of diagnosis, contrary to a study in New York where 53% of these patients were already in advanced stages (IV) at diagnosis, with only 38% in stages I or II.[13]

A study conducted in the North American population[16] reported greater involvement of lung metastasis along with the presence of cervical lymph nodes in young patients, unlike the present study where 70% of patients with thoracic metastasis and cervical lymph nodes were over 55 years old. This difference in results suggests the hypothesis that

TABLA 1. Characteristics of the population with thyroid cancer according to the presence of thoracic metastases

Variable	Total (n = 241)	Thoracic metastases (n = 53)	Without thoracic metastases (n =188)	p
Age in years (SD)	54.0 (14.3)	59.6 (12.7)	52.5 (14.3)	0.0022
Women, n (%)	206 (85.4)	41 (77.3)	165 (87.7)	0.058
Histopathological diagnosis, n (%)				
Papillary	229 (95.0)	48 (90.57)	181 (96.28)	0.11
Follicular	6 (2.5)	1 (1.89)	5 (2.66)	0.12
Medullary	3 (1.24)	1 (1.89)	2 (1.06)	0.211
Anaplastic	1 (0.41)	1 (1.89)	0 (0)	0.22
Follicular and papillary	1 (0.41)	1 (1.89)	0 (0)	0.22
Follicular and medullary	1 (0.41)	1 (1.89)	0 (0)	0.22
Clinical stage, n (%)				
I	158 (69.29)	15 (28.3)	143 (76.0)	<0.001
II	52 (21.58)	21 (39.62)	36 (19.15)	<0.001
III	6 (2.49)	2 (3.77)	5 (2.66)	<0.001
IVA	3 (1.24)	3 (5.66)	3 (1.6)	<0.001
IVB	10 (4.15)	9 (16.98)	1 (0.53)	<0.001
IVC	3 (1.24)	3 (5.66)	0 (0)	<0.001
Weight, M (IQR)	67.5 (60 - 77)	63 (54-71)	68 (61-78)	0.0039
Height, M (IQR)	157 (152- 160)	155 (150-162)	157 (153-160)	0.2843
BMI, M (IQR)	27.4 (24.1- 30)	26.6 (22.2-29.6)	27.63 (24.6-30.1)	0.027
Comorbidities, n (%)				
Arterial hypertension	62 (25.73)	17 (32.08)	45 (23.94)	0.231
Lung disease	8 (3.32)	3 (5.66)	5 (2.66)	0.379
Kidney disease	6 (2.49)	4 (7.55)	2 (1.06)	0.022
Heart failure	3 (1.24)	3 (5.66)	0 (0)	0.01
Cervical lymph node involvement, n (%)	148 (68.84)	43 (86.0)	105 (63.64)	0.003
Exposures, n (%)				
Active smoking	9 (3.73)	5 (9.43)	5 (9.43)	0.027
Previous radiation	2 (0.83)	1 (1.89)	1 (0.53)	0.633
Treatments, n (%)				
Partial thyroidectomy	34 (14.11)	9 (16.98)	25 (13.3)	0.496
Total thyroidectomy	235 (97.51)	51 (96.23)	184 (97.87)	0.615
Lymph node dissection	195 (80.91)	46 (86.79)	149 (79.26)	0.217
Iodine therapy	175 (72.61)	41 (77.36)	134 (71.28)	0.381
Iodine therapy for metastasis	17 (7.05)	13 (24.53)	4 (2.13)	<0.001
Tyrosine kinase inhibitors	6 (2.49)	6 (11.32)	0 (0)	<0.001
Symptoms, n (%)				
Cough	9 (3.73)	5 (9.43)	4 (2.13)	0.027
Dyspnea	11 (4.56)	8 (15.09)	3 (1.60)	<0.001
Sputum	3 (1.24)	2 (3.77)	1 (0.53)	0.2561
Paraclinical tests, n (%)				
Thyroglobulin >38ng/ml	22 (9.61)	17 (34)	5 (2.79)	<0.001
Detection of anti-thyroglobulin antibodies	40 (17.7)	11 (22)	29 (16.48)	

TABLA 2. Variables associated with the presence of thoracic metastases

Variable	OR	CI	P
More than 55 years of age	2.79	1.46-5.33	0.002
Weight < 60 kg	2.17	1.130-4.17	0.019
Thyroglobulin above 38ng/ml	17.9	6.18-51.9	<0.001
Cervical lymph node involvement	3.51	1.48-8.29	0.004
Dyspnea	10.9	2.79-42.9	0.001

in the Latin American population, the behavior of the thyroid carcinoma generates greater involvement in older individuals.

On the other hand, the most reported symptom in our population with thoracic metastasis was dyspnea. No studies were found in the literature that report the symptoms of patients with metastasis. However, a study conducted by Jang et al[17] in patients who underwent iodine therapy for lung metastasis reported that the presence of respiratory symptoms was associated with a decrease in forced vital capacity after the treatment. This highlights the probable need for further studies in this area and the development of a protocol for assessing lung function in patients who are to be treated with radioactive iodine for thoracic and lung metastases.

In terms of follow-up with laboratory studies, thyroglobulin and anti-thyroglobulin antibody tests are of great importance. A Chinese study (Song et al) reported that 83.98% of patients with lung metastasis had thyroglobulin levels above 100 ng/ml.[6] In our study, 34% of patients with thoracic metastasis and only 2.7% of patients without metastasis had thyroglobulin levels of more than 38 ng/ml. This value could be suggested as an estimated cutoff point for metastasis risk in our population.

In our population, it is a challenge to determine if the high prevalence and more frequent involvement in older adults were a result of conducting the study in a cancer reference center.

CONCLUSION

In conclusion, considering the favorable prognosis of non-metastatic thyroid cancer patients and the fact that pulmonary metastasis represents the most common form of progression, it is imperative to continue documenting factors that could be related to or associated with the presence of thoracic metastasis. These factors could potentially serve as markers of specific and earlier interventions in this population. The main strength of this study is the fact that it provides local data on the prevalence of thoracic metastasis and potential associated factors. This could prove valuable for future prospective studies aimed at identifying associated variables and prognostic factors. The disadvantage of this work is that it may be susceptible to classification and information biases stemming from data loss, given the retrospective nature of the study design.

Conflict of interest

The authors have no conflict of interest to declare.

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