



ORIGINAL ARTICLE

Thyroid carcinoma: Description of 634 patients treated at the Hospital Universitario San Ignacio, Bogotá, Colombia

Carcinoma de tiroides: Descripción de 634 pacientes atendidos en el Hospital Universitario San Ignacio, Bogotá, Colombia

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Abstract

Introduction. The incidence of thyroid carcinoma has increased worldwide, probably related to the overdiagnosis of asymptomatic thyroid nodules. The high survival of differentiated thyroid carcinoma has allowed less radical surgical resection or even active surveillance for selected tumors. There are reports of clinicopathological features of thyroid carcinoma in our country that are different from those reported in the international literature.

Methods. Retrospective observational study of a cohort of patients with thyroid carcinoma treated at a university hospital between 2015 and 2020.

Results. 634 patients were identified; 83.4% were female. Total thyroidectomy with central dissection was the most performed procedure (86.7%). Of the 613 differentiated thyroid carcinomas, 94.2% were papillary type, followed by Hürtle cell carcinoma with 1.6%; 26.2% presented aggressive histological subtypes and 28.4% had bilateral tumor involvement. Metastatic disease was found in 58.7% of the central dissections performed, which was 49% in patients with papillary microcarcinomas (19%). Of the 68 recurrent laryngeal nerve injuries, 47% were due to oncological involvement.

Discussion. In our series, the rate of patients with papillary thyroid carcinoma and its aggressive histological subtypes as well as bilateral tumor involvement is higher than that reported in the scientific literature.

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Conclusion. The biological behavior of thyroid carcinoma is variable and may have different characteristics between regions; management in our environment should consider the characteristics of our population.

Keywords: thyroid gland; thyroid neoplasms; papillary thyroid cancer; thyroidectomy; postoperative complications; prognosis.

Resumen

Introducción. La incidencia del carcinoma de tiroides ha aumentado a nivel mundial, probablemente relacionado con el sobre diagnóstico de nódulos tiroideos asintomáticos. La alta sobrevida del carcinoma diferenciado de tiroides ha permitido posibilidades de manejo quirúrgico menos radicales, o inclusive, la vigilancia activa de tumores seleccionados. Existen reportes de características clínico-patológicas del carcinoma de tiroides de nuestro país distintas a las reportadas en la literatura internacional.

Métodos. Estudio observacional descriptivo de una cohorte retrospectiva de pacientes con carcinoma de tiroides atendidos en un hospital universitario entre 2015 y 2020.

Resultados. Se identificaron 634 pacientes, el 83,4 % de sexo femenino. La tiroidectomía total con vaciamiento central fue el procedimiento más realizado (86,7 %). De 613 carcinomas diferenciados de tiroides, el 94,2 % corresponden al tipo papilar, seguido por el carcinoma de células de Hürtle (1,6 %); el 26,2 % presentaron subtipos histológicos agresivos y el 28,4 % compromiso tumoral bilateral. En los vaciamientos centrales se encontró 58,7 % de enfermedad metastásica; que fue de 49 % en los pacientes con microcarcinomas papilares (19 %). De las 68 lesiones del nervio laríngeo recurrente, 47 % fueron por secciones oncológicas.

Discusión. En nuestra serie, la proporción de pacientes con carcinoma papilar de tiroides y de sus variantes histológicas agresivas, así como el compromiso tumoral bilateral es mayor a lo reportado en la literatura científica.

Conclusión. El comportamiento biológico del carcinoma de tiroides es variable y puede tener características diferentes entre regiones; el manejo en nuestro medio debería considerar las características propias de nuestra población.

Palabras claves: glándula tiroides; neoplasias de la tiroides; cáncer papilar tiroideo; tiroidectomía; complicaciones posoperatorias; pronóstico.

Introduction

The incidence of thyroid carcinoma has been increasing in recent years worldwide. By 2020, 5,304 new cases were diagnosed in Colombia, with an incidence of 9.1 per 100,000 inhabitants, ranking fourth in frequency of malignant neoplastic diseases in women in our country¹. The increase in cases, probably related with the overdiagnosis²⁻⁴, the high survival in differentiated carcinomas and the regional differences in histological types, explain the multiplicity of management guidelines that exist on this pathology⁵⁻⁸.

The application of international recommendations has introduced in the management algorithm

the possibility of limited surgical resections⁹⁻¹², and even active surveillance of tumors up to 1.5 cm^{13,14}, with the intention of reducing morbidity derived of surgical management^{13,15,16}. However, a higher percentage of papillary thyroid carcinoma has been reported in Colombia compared to other countries^{17,18}. In addition, there is a higher proportion of aggressive histological variants (29.5%), which are related to a worse prognosis and a higher risk of recurrence^{19,20}. A significant percentage of tumor multicentricity has also been documented, with bilateral involvement of up to 31.7% and, in terms of lymph node involvement, 64.8% of patients have metastatic disease

in the central dissection at the time of surgical management^{19,21}. This, added to the difficulties in monitoring and access to health services in our country, has been the justification for the management of choice for patients diagnosed with thyroid carcinoma in our institution to be an initial aggressive cytoreduction, independent of tumor size.

Methods

A retrospective descriptive observational study was designed whose study population was patients with thyroid carcinoma, who underwent surgical management and follow-up at the Hospital Universitario San Ignacio, in Bogotá, Colombia, between December 2015 and June 2020. The information of the patients was extracted from the SAHI electronic medical record and the registry data is housed in Research Electronic Data Capture REDCap®.

A total of 818 medical records were reviewed, of which 634 met the inclusion criteria. Demographic, cytological (Bethesda classification), histopathological variables, TNM 2017 classification (according to the modifications of the American Thyroid Association)²², structural risk stratification and information on surgical management were considered.

Postoperative hypoparathyroidism was defined as the presence of postoperative intact parathyroid hormone molecule (iPTH) levels <15 pg/mL with semi-automated serum calcium levels <8 mg/dL or ionized calcium less than 1.1 mmol/L, with or no symptoms of hypocalcemia. Transient hypoparathyroidism was defined as resolution of hypocalcaemia within the first 6 months after surgery. For our analysis, the need for calcium supplementation (more than 2 calcium tablets per day) to control symptoms of hypocalcaemia after the sixth month after surgery was also considered a criterion for permanent hypoparathyroidism.

Regarding the statistical analysis, the qualitative variables were described with measures of absolute and relative frequencies, expressed as percentages, and for the quantitative variables measures of central tendency, average and

median, and measures of dispersion were established, according to the distribution of the data.

Results

Of the 634 records of thyroid carcinoma, 529 (83.4%) corresponded to women and the median age at diagnosis was 54.5 years (Table 1). Regarding the health system, 537 patients belonged to the contributory system (84.7%) and 87 to the subsidized system (13.7%), which could influence the time between diagnosis and initial surgical treatment, whose median was 128 days. Of the 447 patients who had preoperative TSH values, 75% were euthyroid at the time of diagnosis. Among the percutaneous fine-needle biopsies

Table 1. Demographic and clinical characteristics of patients diagnosed with thyroid cancer treated at Hospital Universitario San Ignacio, Bogotá, Colombia. n=634.

Characteristic	Frequency (%)
Age	
≥ 55 year-old	315 (49.6)
< 55 year-old	319 (50.3)
Gender	
Female	529 (83.4)
Male	105 (16.6)
Health system	
Contributory	537 (84.7)
Subsidized	87 (13.7)
Others (prepaid medicine, individuals or special systems)	10 (1.6)
Weight	
Median	67 Kg
Range	40-126 Kg
Biopsie (n=482)	
Suspicious thyroid percutaneous or conclusive of malignancy	412 (65)
Other type of lymph node biopsy, thyroid (open approach), lung or bone	70 (11.1)
Preoperative TSH (n=447)	
Euthyroids	335 (75)
Thyroid peroxidase antibody (n=92)	21 (27.6)
Anti-thyroglobulin antibodies (n=75)	26 (34.2)

Source: Own authors.

(FNAB) of the thyroid for preoperative diagnosis, 65% presented suspicious or conclusive cytologies of malignancy according to the Bethesda classification (Table 2).

Nineteen patients (5.2%) required perioperative reintervention associated with complications. In the first 30 postoperative days, 91 patients (14.3%) re-visited the emergency room and hypocalcaemia was the most frequent cause in 8.5% (54 of 634 patients). It was possible to determine in the clinical history that the vast majority of these cases were associated with the non-consumption of routinely formulated calcium supplements.

A total of 138 complications derived from surgical treatment were documented in 108 patients

(17%). Of the 68 lesions of the recurrent laryngeal nerve (RLN) reported in the clinical history (7 bilateral), 32 corresponded to oncological section of the nerve due to tumor infiltration. Excluding the latter from the analysis, 5.6% of the patients presented iatrogenic RLN injury during the surgical procedure (Table 4). 1.2% of patients met the criteria for permanent hypoparathyroidism determined in our study.

Differentiated thyroid carcinoma was diagnosed in 96.6% of the patients. Regarding histological distribution, papillary thyroid carcinoma was the most frequently reported (94.2%), followed by Hürthle cell carcinoma (1.6%) and follicular carcinoma (0.9%) (Table 5). Of the 97 cases with high cell variant, only in 58 patients was a record of the percentage of involvement of this variant found by the pathologist. It will be extended that in 84.5% there was a compromise greater than 10% by this cell type. The median size of the dominant tumor nodule was 1.6 cm (IQR 0.5 - 5).

Multifocality (2 or more foci of carcinoma in the same lobe and/or the isthmus) was identified in 294 cases (46.3%), and involvement of the contralateral lobe (bilaterality) in 180 cases (28.4%). As an additional finding, the presence of chronic lymphocytic thyroiditis was reported in 28.9% of the patients. In 121 patients the tumors were smaller than 1 cm (19.8%); in these cases, multifocality was reported in 34.5%, and bilaterality in 23.4%.

Table 2. Histopathological characteristics of patients diagnosed with thyroid cancer. Bogota, Colombia. n=634.

FNAB* according to Bethesda Ranking	Number of patients (n)	Percentage (%)
FNAB was not performed	32	5.1
Insufficient or hemorrhagic	5	0.8
Normal or goiter	27	4.3
Inflammatory	57	8.9
(indeterminate lesion)		
Follicular lesion with atypia	90	14.2
Suspected of malignancy	201	31.7
Conclusive of malignancy	211	33.3
No data	11	1.7
Total	634	100

* FNAB: Fine needle aspiration biopsy. Source: own authors.

Table 3. Initial surgical management of patients diagnosed with thyroid cancer.

Type of surgery	Frequency (%) n=634
Subtotal thyroidectomy	20 (3.15)
Total thyroidectomy (TT)	57 (8.99)
Oncological thyroidectomy (OT)	454 (71.61)
OT + Unilateral neck dissection (UND)	92 (14.51)
OT + bilateral neck dissection (BND)	4 (0.63)
Other surgery	7 (1.10)

Source: Own authors.

Table 4. Complications derived from surgical treatment presented in 108 patients.

Complication	Frecuencia	% (n=138)	% (n=634)
RLN* unilateral	54	39.1	8.52
RLN* bilateral	7	5.1	1.10
Hypoparathyroidism	54	39.1	8.52
Surgical wound hematoma	6	4.3	0.94
SSI**	4	2.9	0.63
Phonasthenia	4	2.9	0.63
Others	9	6.5	1.42
Total	138	100	21.1

* RLN: recurrent laryngeal nerve injury. ** SSI: Surgical site infection. Source: Own authors

Table 5. Types of thyroid carcinoma and histological variants of papillary carcinoma.

Type of thyroid neoplasm	Frequency	Percentage
Papillary	597	94.2
Hürthle cells	10	1.6
Follicular	6	0.9
Poorly differentiated	7	0.9
Medullary	7	0.9
Anaplastic	3	0.5
Others	4	0.6
Total	634	
Histological variant of papillary cancer		
Classic	327	54.8
Encapsulated follicular	108	18
Infiltrative follicular	49	8.2
Tall cell	97	16.2
Sclerosing	11	1.84
Columnar	1	0.2
Others	4	0.7
Total	597	

Source: Own authors.

Central dissection was performed on 100 of them, with metastatic involvement found in 49%. The median for the number of dissected lymph nodes in the central dissection was seven (IQR 0-26) and for the number of lymph nodes with metastatic involvement in the central dissection was one (IQR 0-21). Metastatic disease was found in 58.7% of central dissections. 53% of the parathyroids were preserved as none were found in the surgical piece. Tumor involvement was found in ten parathyroids (3.4%), being mainly extrathyroidal in location with tumor invasion in 2.7% of patients.

Regarding the distribution of structural risk stratification for tumor relapse according to the ATA 2015 criteria²³, 39.7% of patients were classified as low risk, 38% intermediate risk, and 20.8% high risk.

Discussion

Despite the progressive increase in the incidence of thyroid carcinoma, the mortality associated with this pathology is low and has remained stable. The increase in cases²⁴, probably related to the greater possibility of detecting asymptomatic

nodules smaller than 2 cm by ultrasound, have generated a new therapeutic challenge, which implies defining specific parameters to distinguish aggressive tumors from those with an indolent clinical course. to avoid overtreatment and adequately identify patients who require more aggressive management of their disease²⁵⁻²⁷. In this sense, advances in the understanding of the molecular biology of thyroid cancer have made it possible to identify genetic mutations that can be used in the decision-making process^{28,29}; however, in developing countries, access to molecular studies is very limited.

Our objective was to describe the clinical and histological characteristics of patients with thyroid carcinoma and the outcomes of surgical procedures performed in a high-volume center in the last 6 years. We consider that these findings should, bring at least into question the applicability of international guideline recommendations in patients with different epidemiological characteristics, when defining the best initial treatment therapy and the most appropriate follow-up for each of them.

Limited resections, with or without dissection of the upper mediastinum, or active surveillance of tumors up to 1.5 cm in selected patients, are new alternatives in the management algorithm that emerged with the intention of reducing the morbidity of surgical management, especially related to RLN injury³⁰, the need for indefinite hormonal therapy and postoperative hypoparathyroidism³¹. It is important to highlight that, for this type of decision, an adequate initial staging is needed and, as far as possible, define the behavioral characteristics thyroid cancer oncology (molecular tests) from the preoperative period^{32,33}, and guarantee strict clinical and paraclinical follow-up, conditions that are difficult to comply with in our country. For this reason, the adequate characterization of the histopathological variables of the population has been and will continue to be a determining factor in defining the applicability of the different international guidelines in our setting.

Several series of cases have been reported in Colombia, with clinical-histopathological variables that correspond to those found in this group of pa-

tients, including a higher proportion of papillary carcinoma, with a higher percentage of aggressive histological variants and with bilateral tumor involvement in 1 out of 3 patients^{17-19,34}. In this study, thyroid carcinoma was the most frequent, with a frequency of 97%, and papillary carcinoma represented 94.2%, a higher percentage than that reported in the world literature, which is estimated to be 85%³⁵. Regarding histological variants, as a relevant and consistent data with case series from our country, aggressive histological subtypes were present in 26.4%, a higher percentage than the 10% reported in publications from the US and Europe. The tall cell and follicular infiltrative variants of papillary carcinoma accounted for the majority of these cases. Additionally, multifocality and bilateral tumor involvement were evidenced in 46.3% and 28.4% of the cases, respectively.

The size of neoplastic lesions is decreasing at the time of diagnosis. The World Health Organization (WHO) has defined papillary thyroid tumors smaller than 1 cm as papillary thyroid microcarcinoma (PTMC)³⁶. Initial reports of incidence were 25%; however, in the 21st century increased up to 39%, mainly due to the application of much more sensitive diagnostic tools and their indiscriminate use by health personnel⁴. When evaluating the 121 PTMCs in our series, multifocality of 34.5% was found, a percentage of bilaterality of 23.4% and 50% positive nodes of the 100 central dissections that were performed in these patients. Although they are described as lesions with a good prognosis³⁷, this information could be essential to determine the extent of the initial surgery in our environment.

There is currently controversy about prophylactic central emptying^{8,10,17}, taking into account that in some studies they do not alter the course of the disease and long-term survival. Its main indication is in advanced tumors or in clinical lymphatic involvement^{27,33,38}. The prevalence of metastatic involvement in our patients was 58%. Although the objective of this study is not to determine the impact of these results on prognosis and tumor relapse, the behavior of these determining factors and their impact on the initial therapeutic approach are still important.

RLN injury, performed due to tumor involvement were excluded from the analysis, was 5.6%, permanent hypoparathyroidism 1.2%, and the frequency of surgical wound hematoma was less than 1%. It is important to highlight that, although total thyroidectomy with central dissection was performed in the vast majority of cases as the initial treatment of choice, regardless of tumor size, the complications identified in this group of patients are found in percentages similar to those reported in the literature by high-volume head and neck cancer surgery centers^{14,39-42}.

The limitations of this study are those inherent to its retrospective nature. Similarly, the high variability in pathology reports, as well as the lack of unification of concepts at the time of defining the histological and clinical characteristics in some cases, such as the criteria for permanent hypothyroidism, may affect the results obtained.

Conclusion

The biological behavior of thyroid carcinoma is variable and may have different characteristics between populations. Although it is not the main objective of this study to determine the oncological results, the findings described in our patients with thyroid carcinoma have been considered sufficient reasons to routinely perform aggressive initial cytoreduction (oncological thyroidectomy). Morbidity rates are acceptable and comparable to those reported in the literature. Our hypothesis is that, taking into account the clinical-histopathological characteristics and the difficulties in follow-up, this approach allows adequate oncological control from the first moment of management. The results of follow-up and survival will be the subject of another study of this population.

Compliance with ethical standards

Informed consent: This study is considered a non-risk research according to Resolution 008430 of 1993 of the Colombian Ministry of Health, therefore, informed consent is not required. The design and methodology were approved by the Institutional Ethics Committee of the Hospital Universitario San Ignacio and the Pontificia Universidad Javeriana.

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Author's contributions:

- Conception and design of the study, Acquisition of data: Gabriel Sánchez, Isabel Ángel, Aníbal Ariza.
- Data analysis and interpretation: Gabriel Sánchez, Melissa Díaz, Isabel Ángel, Aníbal Ariza.
- Drafting the manuscript: Gabriel Sánchez, Isabel Ángel, Aníbal Ariza.
- Critical review: Gabriel Sánchez, Melissa Díaz, Isabel Ángel, Aníbal Ariza.

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