

# Post-surgical complications in thyroidectomy patients with thyroid carcinoma

Gabriela Mintegui\*, Zara Martínez

Academic Unit of Endocrinology and Metabolism, Faculty of Medicine, Manuel Quintela Clinical Hospital, University of the Republic, Montevideo, Uruguay.

\*Corresponding author.

Email address: [gabymin92@gmail.com](mailto:gabymin92@gmail.com)

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**Abstract:** Differentiated thyroid cancer (DTC) is the most common endocrine neoplasia, with an increasing incidence worldwide. Total thyroidectomy (TT) is one of the most important pillars of treatment; however, it is not without complications. Of these, the most common are transient/permanent hypoparathyroidism, recurrent laryngeal nerve (RLN) injury, and postoperative hemorrhage. Objective: To determine the prevalence of overweight and obesity in this population and some risk factors for this type of tumor. To determine the incidence of postoperative complications after TT as the initial treatment for DTC. Materials and methods: An observational, descriptive, and retrospective study conducted at the Academic Unit of Endocrinology and Metabolism between 2011 and 2021. Quantitative variables were represented by mean and median; qualitative variables were described as absolute and relative frequencies. Results: 34% were smokers, 39% were overweight, 30% were obese, 7% had a family history of thyroid cancer, and 2% had a history of head and neck radiation. In turn, 59% of the sample presented postoperative complications (71 events in 60 patients). The most frequent complication was transient hypoparathyroidism, present in 48%, followed by permanent hypoparathyroidism (8.9%); 8% presented recurrent laryngeal nerve injury, and 3% presented bleeding; finally, only one patient had a cervical hematoma. Conclusions: The prevalence of overweight/obesity was high in more than half of the cases, and smoking was present in one-third of the patients. Postoperative complications were present in most subjects. Transient hypoparathyroidism was the most common in almost half of them, followed by permanent hypoparathyroidism and, to a lesser extent, RLN injury, surgical site bleeding, and cervical hematoma.

**Key words:** thyroid cancer; postoperative complications; thyroidectomy; hypoparathyroidism

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## 1 Introduction

Thyroid cancer (TC) is the most common endocrine neoplasia. In recent years, its incidence has increased worldwide; this may be associated with the widespread use of imaging studies, particularly ultrasound, and improved equipment. This pathology accounts for 1% to 2% of all cancers. In Uruguay, its incidence is 13.2% per 100,000 inhabitants [1]. In general, it presents a benign behavior, but in isolated cases it can have a poor prognosis [2], which depends on several factors, including pathological variants [3].

Regarding its development, there are several risk factors associated with it, such as radiation, mainly to the head and/or neck, the more clearly defined environmental incidence, and a sedentary lifestyle linked to overweight or obesity—

which produces a pro-inflammatory state and oxidative stress—also related to an increased risk of TC. Also, smoking as a risk factor postulates that tobacco components cause rearrangements in DNA that determine genetic changes, predisposing people to develop these tumors. Other factors such as gender, which indicates the appearance of TC in women three times more than in men for reasons that are still unclear; age, which, although thyroid cancer can occur at any age, appears more frequently in women between 40 and 59 years, and in men, the risk of incidence peaks between 60 and 79 years. Although the genetic bases for these tumors are not entirely clear [4], a history of TC in first-degree relatives (FDRs) could be an important risk factor in patients.

On the other hand, differentiated thyroid carcinoma (DTC) arising from the follicular epithelium is the most common, accounting for approximately 95% of cases. Although it affects all ages, it is more prevalent between 25 and 65 years of age and in women, with a ratio of 4 to 12. It is generally asymptomatic and usually presents as a thyroid nodule detected during physical examination or by various radiological methods requested for another reason. Thyroid nodules are evaluated with ultrasound, and, depending on the characteristics and size, a cytological study is performed using fine-needle aspiration (FNAB) [5]. Regarding the pathological variants of DTC, there are two types: papillary carcinoma (PTC), which represents 80%, and follicular carcinoma (FTC), the second most common, occurring at 6% to 10% [3].

The mainstays of treatment are thyroidectomy, radioiodine, and hormone suppression therapy with levothyroxine [6]. The main objective of surgery is to remove the macroscopic primary tumor. The procedure requires the surgeon's skill to perform it and reduce postoperative complications that affect the prognosis [7]. In addition to identifying the recurrent laryngeal nerve (RLN) and the superior laryngeal nerve (SLN), it is necessary to take into account normal variations in the location and number of parathyroid glands to avoid postoperative hypoparathyroidism [8]. Particularly in Uruguay, a small country, we do not have high-volume surgeons. They average approximately 150 neck surgeries per year, and therefore, morbidity may be higher.

There are two possible surgical procedures for DTC: total thyroidectomy (TT) – or near-total thyroidectomy – and unilateral lobectomy and isthmectomy. A third option, subtotal thyroidectomy, is considered an inadequate procedure and is not recommended. TT involves the removal of all thyroid tissue while attempting to identify and preserve the recurrent laryngeal nerve (RLN), the superior laryngeal nerve (SLN), and the vascular supply to the parathyroid glands [8]. Reported rates for each complication vary by geographic region and are lower in patients operated on by high-volume surgeons and/or at high-volume centers [9,10]. In this regard, one study concluded that the likelihood of experiencing complications after a total thyroidectomy began to decrease once the surgeon performed more than 25 of these total procedures per year [11].

Transient or permanent hypoparathyroidism is the most frequent complication of total or near-total thyroidectomy. In the first case, its frequency varies from 6.9% to 46% [6], depending on the cutoff point used for hypocalcemia, and in the second case, it depends on whether a period of 6 months or 1 year is considered for defining permanent hypoparathyroidism. Transient hypoparathyroidism occurs in up to 20% of patients after surgery for thyroid cancer [12], and permanent hypoparathyroidism occurs in 0.8% to 3% of them after total thyroidectomy [9,12].

Another of the most feared complications of thyroidectomies is recurrent laryngeal nerve (RLN) injury, with an incidence of 3% to 4% [13]. Occasionally, these nerves must be intentionally sacrificed due to direct tumor invasion of the nerve or surrounding tissues. Postoperative unilateral recurrent laryngeal nerve paresia was diagnosed in 3.9% of cases and bilateral paresia in 0.2% [14]. The injury causes the ipsilateral vocal cord to be paralyzed in a paramedian or lateral position. This means that the intrinsic muscles of the larynx, with the exception of the cricothyroid muscle, are denervated, and the patient may experience difficulty swallowing and an increased risk of aspiration [15].

Postoperative hematoma is a rare but potentially fatal complication of thyroid surgery. To prevent it, meticulous hemostasis remains crucial [16]. Regarding the prevention of postoperative bleeding and hematoma formation, patients should discontinue all anticoagulants before surgery; hemostasis must be meticulously maintained throughout the procedure. Furthermore, certain conditions have been associated with the development of postoperative hematomas, such as inflammatory thyroid disease, partial thyroidectomy, and the use of drains [17].

This study determined the prevalence of postoperative complications associated with thyroidectomy as a treatment for differentiated thyroid cancer (DTC), as these complications are a significant cause of morbidity and reduced quality of life for patients. The study also determined the prevalence of certain risk factors that may contribute to the development of these tumors, such as smoking, overweight, a family history of thyroid cancer, and exposure to radiation in the head and neck. It is worth noting that there are no recent publications from other healthcare centers in the country on this topic. Furthermore, worldwide, lobectomy or active surveillance is suggested for tumors up to 1.5 or 2 cm, because more extensive procedures increase the risk of morbidity, and these types of tumors generally do not increase mortality.

## **2 Ethical standards**

The study was approved by the Ethics Committee of the Hospital de Clínicas with resolution number 38-22.

## **3 Statistics**

This was an observational, descriptive, retrospective study conducted at the Academic Unit of Endocrinology and Metabolism of the Hospital de Clínicas (Dr. Manuel Quintela) in Montevideo, Uruguay, between January 2011 and January 2021.

Patients included were those diagnosed with DTC, aged 18 years or older, who received care at the center during the study period. The initial sample consisted of 207 patients with a diagnosis of DTC; however, 79 were excluded due to loss to follow-up at our center, and 27 did not participate due to a lack of required data. Therefore, the final number of participants was 101.

To conduct the study, data was collected from medical records including demographic information, personal history (smoking, overweight, obesity, head and neck radiation), and postsurgical complications (transient or permanent hypoparathyroidism and recurrent laryngeal nerve injury).

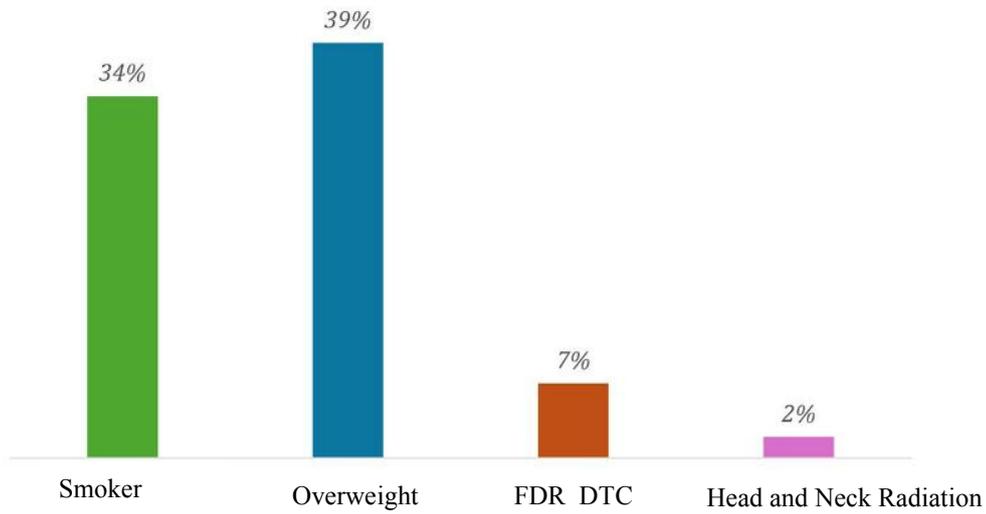
It is important to clarify that hypoparathyroidism was considered in patients who presented with calcium levels greater than or equal to 8.5 mg/dL and/or symptoms of hypocalcemia (cramps, paresthesias, positive Trousseau's sign). Transient hypoparathyroidism was defined as occurring during the first year after surgery, while permanent hypoparathyroidism was defined as persisting despite treatment for hypocalcemia after that time. Recurrent laryngeal nerve (RLN) damage was noted when direct laryngoscopy revealed paralysis of at least one vocal cord up to 12 months after surgery. Hemorrhage or hematoma were recorded as present only if they were described in the patient's postoperative medical record.

Quantitative variables were represented using the mean and median as measures of central tendency, while dispersion was represented by the standard deviation and range. Qualitative variables were described using absolute and relative percentage frequencies. All statistical tests performed were two-tailed, and p-values less than 0.05 were considered statistically significant. Statistical analysis was performed using JASP v0.16 statistical software, JASP Team (2023), and GraphPad Prism v8.4.3 (2020).

## **4 Results**

A total of 101 patients were included, the majority of whom were female, with an average age at diagnosis of 40 years. It is also noteworthy that a large percentage had a high BMI (Table 1). Regarding the risk factors considered for the

development of carpal tunnel syndrome, smoking and overweight/obesity were the most relevant, accounting for almost 40% and 30%, respectively (Figure 1).



Graph 1. Frequency of risk factors for DTC

Table 1. Description of the patients in the sample

	Total (N=101)
<b>Sex</b>	
Female	93 (92.1%)
Male	8 (7.9%)
<b>Age (years)</b>	
Mean (SD)	49.3 (15.4)
Median [Min, Max]	48 [21, 84]
<b>Age at diagnosis (years)</b>	
Mean (SD)	41.7 (15.4)
Median [Min, Max]	42 [13, 73]
<b>Weight (kg)</b>	
Mean (SD)	73.4 (17.6)
Median [Min, Max]	68.5 [42, 129]
<b>Height (cm)</b>	
Mean (SD)	160 (100)
Median [Min, Max]	160 [150, 180]
<b>BMI (kg/m<sup>2</sup>)</b>	
Mean (SD)	28.4 (6.5)
Median [Min, Max]	27.1 [18.3, 47.7]

Regarding the type of surgery, 95% underwent total thyroidectomy, 3% had a lobectomy, and 2% had a lobectomy and isthmectomy. As for postoperative complications, nearly half of the sample experienced transient hypoparathyroidism, less than 10% of the participants still had hypoparathyroidism after the first year following surgery, and a smaller percentage experienced recurrent laryngeal nerve injury, hemorrhage, or hematomas (Figure 2). There were no cases of bilateral recurrent laryngeal nerve paralysis. Regarding the histopathology, 89% were papillary carcinoma and 11% were follicular carcinoma.

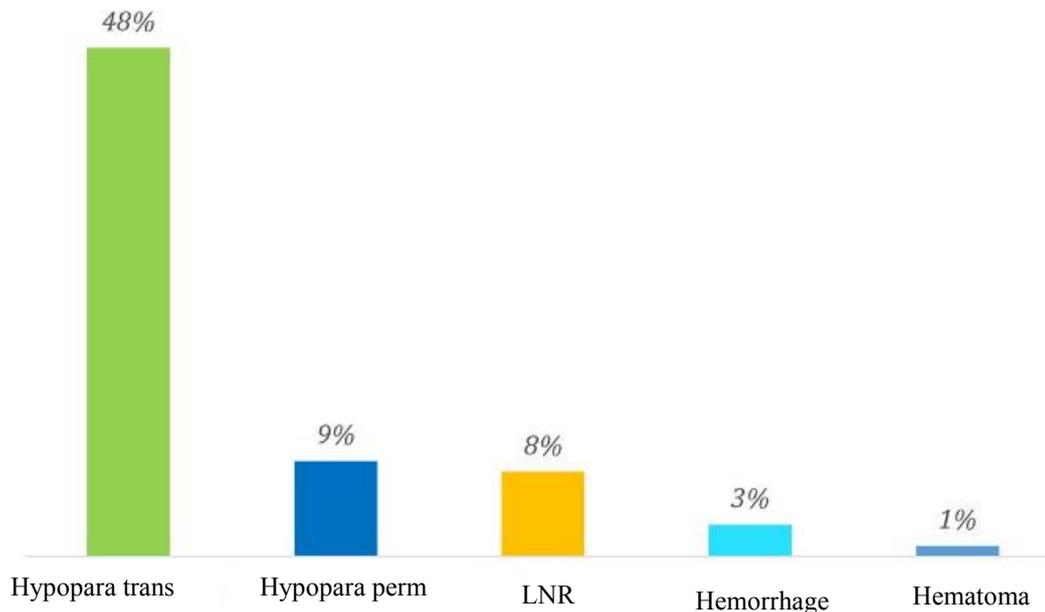


Figure 2. Frequency of postoperative complications

The dataset supporting the results of this study is available in the data repository.

## 5 Discussion

92.1% of the patients were female, and the average age at diagnosis was 42 years, with a median age ranging from 13 to 73 years. This high prevalence in females was established by the American Cancer Society in 2015, and it has been suggested that thyroid cancer, like thyroid nodular disease, occurs approximately three times more frequently in women for reasons that are not yet clear. Similarly, the most frequent age range for diagnosis in this group was between 40 and 59 years, a finding also demonstrated in the present study. Our results are consistent with those of the study by Carles Zafón et al.[18], conducted in Catalonia. This study was carried out with a population similar to ours, where 89% of the patients were female, with a mean age at diagnosis of 44 years. It is also similar to the study by Nelson Arias [19], conducted in Colombia, which analyzed 672 patients, 85% of whom were female with a mean age at diagnosis of 51 years. Another similar study in Latin America is that of Chala [20], which included 84% female patients and 16% male patients, with a mean age of 46 years, very similar to ours.

We found a population with an average BMI in the overweight range, meaning that between 30% and 40% were obese. This reflects the composition of our general population and is consistent with research conducted by the Ministry of Public Health in our country. It is worth mentioning the ENFRENT study from 2013, which included both sexes and concluded that 34.8% were overweight and 23.7% were obese[21]. Therefore, we emphasize that the risk of colorectal cancer appears to increase with a higher body mass index [4].

Another important risk factor for developing TC is a family history of this disease in first-degree relatives. In our study, 7% had this condition, which is consistent with the results of the study by Alma Vidaurri [22], conducted in Mexico, where 44 patients were evaluated, of whom 6.8% had a family history of CTD, and with the study by Gonzalez et al [23], where 8% of their patients had a family history. This can be attributed to the existence of mutations in the genes found on chromosome 19 and chromosome 1, related to a series of family cases [3].

In 96% of the sample, a total thyroidectomy was performed. The results were similar to those found in the study by Andrés Chala et al [20], where 94% underwent total thyroidectomy. However, they differ from the study conducted by Vidaurri [22], who performed this type of surgery in only 63% of patients with thyroid cancer. In patients with differentiated thyroid cancer (DTC), total thyroidectomy is the surgery of choice in many cases, because the procedure offers a lower recurrence rate, better survival, and greater effectiveness with radioiodine therapy, facilitating follow-up with biochemical markers such as thyroglobulin and anti-thyroglobulin antibodies. Nevertheless, the surgical approach depends on the extent of the disease (size of the primary tumor, extrathyroidal extension, or lymph node metastases), the patient's age, and the presence of comorbid conditions [8].

In tumors measuring 1 to 4 cm without extrathyroidal extension and without lymph node involvement, the initial surgical procedure can be either total thyroidectomy or lobectomy. Total thyroidectomy is chosen based on patient preference, the presence of thyroid nodules in the contralateral lobe, metastatic lymph nodes, or the treating team's decision that radioactive iodine therapy may be beneficial as adjuvant therapy or to facilitate follow-up [8]. On the other hand, in the case of tumors larger than or equal to 4 cm, extrathyroidal extension, or distant metastases, a total thyroidectomy is recommended. However, for patients with a history of head and neck radiation in childhood, regardless of tumor size, total thyroidectomy should be performed given the high rate of tumor recurrence when less extensive surgeries are performed [8,24].

Regarding postoperative complications, the most common is hypoparathyroidism, with a prevalence that varies depending on the geographical area. In this study, transient hypoparathyroidism was observed in 48% of cases, which differs from the findings of the study by Joao Goncalvez et al [25], conducted in São Paulo, Brazil, with a similar follow-up period to ours, which reported transient hypoparathyroidism in 13.1% of cases. However, that study included both benign and malignant pathology, and it does not specify the cut-off point used for hypocalcemia. This research also differs from the results of the study by Mintegui et al. [26], conducted at our hospital between 2011 and 2019, with a total of 202 patients, in which 75.7% of them presented this complication. Similarly, another study was conducted at our center in 2020, covering the previous six years. It found that 95% of patients presented with hypocalcemia in the first 72 hours and 6% with permanent hypoparathyroidism [27].

We attribute these differences to the fact that our center is a university hospital and we do not have high-volume surgeons, and also that our research included only patients with total thyroidectomy for differentiated thyroid cancer. This is unlike the other three studies mentioned, in which total thyroidectomy was performed for both benign and malignant pathology. However, we observed a reduction in the prevalence of this complication compared to previous years at our own center [26]. In our opinion, this may be due to the creation and operation of the Endocrine Surgery Unit since 2019, with a multidisciplinary team that discusses all aspects of the treatment and has standardized the management of these patients with strict follow-up.

Permanent hypoparathyroidism occurred in 8.9% of patients, which is slightly higher than the percentage reported years ago in the Mintegui study [26], which found a permanent hypoparathyroidism incidence of 7.3%, and the Pitoia report [28], conducted in Argentina, with a similar geographic area and population to ours, which found permanent

hypoparathyroidism in 5.7% of patients. We believe that the increased frequency of this complication in our center may be due to the sample size. Furthermore, the previous study included patients with thyroidectomy for benign and malignant conditions, while this study only included patients with differentiated thyroid carcinoma (DTC), who require more extensive and complex surgeries, generally including lymph node dissection. All of these factors may increase the risk of this complication. This also differs from the findings of the Chala study [20], in Colombia, which involved 12 years of thyroidectomies for DTC, where permanent hypoparathyroidism occurred in 1.1%.

Iatrogenic injury to the recurrent laryngeal nerve is one of the most concerning complications of thyroid surgery. In several studies, rates ranged from 0% to 7.1% for transient injury and from 0% to 11% for permanent injury; surgeons with higher volumes achieved lower injury rates. If the vocal cord remains immobile for more than one year, permanent paralysis is likely to occur [15]. RLN injury causes paralysis of the ipsilateral vocal cord, which is then positioned paramedially or laterally. Medialization of the affected vocal cord improves both swallowing and phonation by allowing the functional contralateral vocal cord to close the larynx. However, bilateral vocal cord paralysis, due to injury to both recurrent nerves, is a rare (0.4%) but devastating complication of total thyroidectomy that occurs most frequently in reoperations [8]. In our sample, there were no patients with bilateral paralysis. In our study, recurrent laryngeal nerve (RLN) injury occurred in 7.9% of patients. These findings are higher than those reported by Fretes et al. [29] in Paraguay, with an incidence of 4.5%, and also higher than that reported by Chala, who reported recurrent laryngeal nerve injury in 0.9% [20].

Regarding hematoma, it occurred in only 1% of cases, a figure similar to other studies. In a retrospective review of 150,012 patients, 1.25% developed a postoperative hematoma, while in other studies the rate ranged between 0.7% and 1.5% [30].

Follicular thyroid cancers are more common in areas of the world where people's diets are low in iodine. Conversely, a diet high in iodine can increase the risk of papillary thyroid cancer. Uruguay, in particular, is included in the iodine-sufficient areas where most people obtain sufficient amounts of this mineral in their diet and where it is also added to table salt [4]. Our pathology results reflect this fact. We found 89% papillary thyroid carcinoma (PTC) and 11% follicular thyroid carcinoma (FTC), comparable to Colombia, where Chala [20] found a distribution of 87% papillary carcinoma and 7.7% follicular carcinoma.

To minimize the risks of surgical procedures performed in these cases, several technical resources can be used, such as the use of magnifying lenses during surgery and recurrent laryngeal nerve monitoring—which is not available in the vast majority of centers in our country. To prevent hypoparathyroidism, parathyroid localization using immunostaining is helpful, as is the use of local coagulation adjuvants or coagulants to reduce the incidence of bleeding and/or hematomas.

## **6 Conclusions**

The prevalence of overweight/obesity was high in more than half of the sample. Smoking was present in one-third of the patients. At least one postoperative complication occurred in the majority. Transient hypoparathyroidism was the most common, occurring in almost half of the patients, followed by permanent hypoparathyroidism and, to a lesser extent, recurrent laryngeal nerve (RLN) injury, surgical site hemorrhage, and cervical hematoma. In our center, this study showed a lower rate of transient hypoparathyroidism than other studies.

## **Conflicts of Interest**

The author declares no conflicts of interest regarding the publication of this paper.

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### **Ethical responsibilities**

The study was approved by the Ethics Committee of the Hospital de Clínicas under resolution number 38-22.

## **Author Contributions**

Gabriela Mintegui: Conceptualization, data curation, formal analysis, fundraising, research, methodology, project management, resources, supervision, validation, visualization, drafting, revision, and editing.

Zara Martínez: Conceptualization, data curation, formal analysis, fundraising, research, methodology, project management, resources, supervision, validation, visualization, drafting, revision, and editing.