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RESEARCH

Large goiters and postoperative complications: does it really matter?

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Abstract

Introduction Thyroidectomy is one of the most commonly performed surgical procedures worldwide. Although the mortality rate is currently approaching 0%, the incidence of complications in such a frequent surgery is not insignificant. The most frequent are postoperative hypoparathyroidism, recurrent injury, and asphyxial hematoma. The size of the thyroid gland has traditionally been considered one of the most important risk factors, but there is currently no study that analyzes it independently. The objective of this study is to analyze whether the size of the thyroid gland is an isolated risk factor for the development of postoperative complications.

Patients and method A prospective review of all patients who underwent total thyroidectomy at a third-level hospital between January 2019 and December 2021 was conducted. The thyroid volume was calculated preoperatively using ultrasound and, together with the weight of the definitive piece, was correlated with the development of postoperative complications.

Results One hundred twenty-one patients were included. When analyzing the incidence of complications based on the quartiles of weight and glandular volume, there were no significant differences in the incidence of transient or permanent hypoparathyroidism in any of the groups. No differences were found in terms of recurrent paralysis. No fewer parathyroid glands were visualized intraoperatively in patients with larger thyroid glands, nor did the number of them accidentally removed during surgery increase. In fact, a certain protective trend was observed with regard to the number of glands visualized and glandular size or in the relationship between thyroid volume and accidental gland removal, with no significant differences.

Conclusion The size of the thyroid gland has not been shown to be a risk factor for the development of postoperative complications, contrary to what has traditionally been considered.

Keywords Thyroidectomy · Goiter · Complications · Hypoparathyroidism · Recurrent injury

Introduction

Thyroidectomy is one of the most commonly performed surgical procedures worldwide. Surgery of the thyroid began in the mid-eighteenth century, with very high complication rates and a mortality rate close to 40%, primarily due to post-surgical bleeding or secondary suffocation from airway obstruction [1]. Starting in the nineteenth century, Theodor Kocher described his meticulous technique of thyroidectomy with a substantial improvement in results and a drastic reduction in mortality [2], which has been maintained and even improved over time. Today, it is considered a safe surgery, with a very low mortality rate if performed by expert surgeons [3–5].

Although over the years mortality has approached 0%, the incidence of complications in such a frequent surgery is a cause for concern and, at times, legal issues. Although there

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are other complications, the most frequent are post-surgical hypoparathyroidism, recurrent laryngeal nerve injury, and asphyxial hematoma. The incidence recorded in the literature is variable, from 40–50% of transient hypoparathyroidism in total thyroidectomies to 3–5% in the case of permanent hypoparathyroidism, or up to 1–3% when we talk about definitive recurrent laryngeal nerve injury or bleeding [6, 7].

Precise knowledge of cervical anatomy and a careful surgical technique when performing thyroid surgery are essential to minimize these potential complications, although it is true that there are factors that do not depend on the surgeon and that have traditionally been described as potentially risky. Of these, the size of the goiter has always appeared as one of the most important, without any studies evaluating it independently [7–9].

The objective of this study is to analyze if the size of the thyroid gland is an independent risk factor in the development of post-surgical complications, primarily post-surgical hypoparathyroidism, given its frequency and impact on the patient's quality of life, since its prevention is of great importance.

Patients and method

A prospective review of all patients who underwent total thyroidectomy in a reference hospital between January 2019 and December 2021 was conducted. The study was approved by the Ethics Committee of the Ramón y Cajal University Hospital Research with registration number 348/20. All procedures performed with human participants were in accordance with the ethical standards of the research committee and the Declaration of Helsinki of 1964 and its subsequent amendments or comparable ethical standards.

Inclusion criteria

The inclusion criteria are as follows: patients over 18 years of age who underwent total thyroidectomy and had a preoperative ultrasound in the 6 months prior to surgery with a complete measurement of the thyroid gland. All patients must have had a postoperative follow-up of at least 1 year, through blood tests with calcium and PTH levels, and vocal cord mobility assessment.

Exclusion criteria

All patients with a history of previous thyroid or parathyroid surgery, those with an inadequate ultrasound assessment of the thyroid gland for the purpose of the study, or those who did not comply with the appropriate follow-up period were excluded. In addition, all patients with preoperative phosphocalcemic metabolism disorders were excluded for a correct assessment of postoperative hypoparathyroidism, as well as those in whom cervical lymphadenectomy was associated.

Method

In all patients who underwent total thyroidectomy, the thyroid volume (ml) was calculated using the ellipsoid formula with a correction factor (length × width × thickness × 0.52) of each thyroid lobe, and the size of the isthmus was also added.

The technique used in all cases was an extracapsular total thyroidectomy with harmonic scalpel and visualization of both recurrent laryngeal nerves with verification by intraoperative intermittent neuromonitoring. At least the upper parathyroid glands were systematically searched. No autofluorescence or indocyanine green device was used. Despite the size of some of the thyroid glands and the fact that, in some cases, they had a certain intrathoracic extension, an extracervical approach was not necessary in any case for their removal.

In all cases, postoperative PTH and calcium were determined 24 h after surgery, with postoperative hypoparathyroidism defined as PTH < 15 pg/ml 24 h after surgery. Transient postoperative hypoparathyroidism was considered in those cases in which, during the first year of follow-up, PTH levels returned to normal. After 1 year of follow-up with PTH levels < 15 pg/ml, it was considered as definitive hypoparathyroidism.

In all patients, vocal cord mobility assessment was performed 1 month after surgery, and in the case of vocal cord paralysis, different controls were performed until recovery or not at 1 year after surgery. Other demographic, intraoperative, immediate postoperative, and follow-up variables were also collected.

Weight of the gland described in the final anatomic pathology report was recorded. When analyzing the results, both the total volume of the gland and the weight of the surgical piece were considered.

Statistical analysis

Quantitative variables that follow a normal distribution are characterized by the mean, standard deviation, and range of values. Quantitative variables that do not follow the Gaussian distribution will be defined by the median as a measure of central tendency and the interquartile range. Normality was checked using the Shapiro-Wilk test. Qualitative variables are defined by the number of cases and the percentage.

To perform the comparison of two discrete variables, the chi-squared test will be used. When the expected value in one of the contingency table cells is below 5, Fisher's exact test will be used for measurement. Student's *t*-test will be used to analyze the comparison of quantitative variables with qualitative variables for independent samples (comparison of 2

means). The comparison of more than two means of quantitative variables with qualitative variables will be performed using the analysis of variance (ANOVA) technique, provided that the quantitative variables follow a normal distribution. In situations where quantitative variables do not follow a normal distribution, the Mann-Whitney test will be used to compare two means and in the case of comparing more than two means, the Kruskal-Wallis test will be used. The Pearson correlation method will be used for the analysis of two normal quantitative variables, while when one or both of the variables do not follow a normal distribution, the Spearman correlation coefficient will be used.

For the analysis, the sample was divided by quartiles of volume measured by ultrasound and was compared with the most frequent postoperative complications such as the number of parathyroids visualized in surgery or accidentally removed, identified later in the surgical piece.

Values of $p < 0.05$ will be considered significant. The SPSS statistical software version 23.0 (SPSS Inc., Chicago, IL, USA) was used for the statistical analysis.

Results

Finally, 121 patients were included in the study, who met the inclusion criteria. In all cases, the surgical technique performed was total thyroidectomy. The demographic characteristics, intraoperative, and immediate postoperative variables of the total patients are shown in Table 1. There was a clear predominance of women (80%) and with a majority diagnosis of multinodular goiter (75%). Due to the COVID pandemic, the number of patients who were operated on or who completed the follow-up during this period was lower than expected. Table 2

When analyzing the different factors based on these quartiles, it was observed that only differences were in terms of gender (more males in Q4) and regarding the definitive histology (more tumors in Q1). There were no statistically significant differences in terms of the incidence of transient or permanent hypoparathyroidism in any of the distribution groups. There were also no differences in cases of recurrent paralysis or postoperative wound infection. There was no decrease in the number of parathyroid glands visualized during the intervention of larger thyroid glands, or an increase in the number of the same accidentally removed identified later in the piece (Table 3).

Postoperative hypoparathyroidism and thyroid volume

The possible factors associated with the development of transient and permanent postoperative hypoparathyroidism have been analyzed. Regarding the first, it was observed that the only difference between patients who developed it was the number of glands visualized and removed during surgery, but not the volume of the thyroid gland (28.2 ml (28–43) vs 32 ml (20–61), $p = 0.525$) (Table 4). These same findings were observed for permanent hypoparathyroidism (28.9 ml (28–55) vs 29.9 ml (20–53), $p = 0.982$).

In addition, when analyzing the median volume by quartiles, it was seen that in three of the four groups (Q1, Q2, and Q4), patients with early hypoparathyroidism had a lower median thyroid volume. However, these differences were not statistically significant (Fig. 1).

Thyroid volume and accidental removal of parathyroid glands

When comparing the accidental removal of parathyroids and the size of the thyroid gland, it was observed that

Table 1 Global characteristics of the sample

	$N = 121$
Gender	
Male	24 (19.8%)
Female	97 (80.2%)
Age (yo)	57.12 ± 15
Diagnosis	
Multinodular goiter	91 (75.2%)
Thyroid cancer	11 (9.1%)
Graves disease	19 (15.7%)
Parathyroid glands visualized	
0	2 (1.7%)
1	12 (10.1%)
2	42 (35.3%)
3	39 (32.8%)
4	24 (20.2%)
Parathyroid glands removed	
0	87 (72.7%)
1	28 (23.1%)
2	5 (4.1%)
Parathyroid glands visualized (location)	
Superior	8 (26.7%)
Inferior	19 (63.3%)
Both	3 (10%)
Length of stay (days)	1.62 ± 1.3
Bleeding	0
Definitive nerve paralysis	3 (1.25%)
Postsurgical hypoparathyroidism	
Transient	44 (36.4%)
Permanent	7 (5.8%)
Wound infection	4 (3.3%)

Table 2 Thyroid gland size

	Median	First quartile (Q1)	Second quartile (Q2)	Third quartile (Q3)	Fourth quartile (Q4)
Patients (number)		30	31	31	29
Volume (ml)	29.01	< 19.32	19.33–29	29.1–55.2	55.3
Weight (g)	55	< 30	31–55	56–99	> 100

Table 3 Characteristics of the sample depending on the volume

Quartile (patients)	Q1 (30)	Q2 (31)	Q3 (31)	Q4 (29)	*P*
Gender (males)	**4 (13.3%)**	**1 (3.2%)**	**7 (22.6%)**	**12 (41.4%)**	**0.002**
Age (yo)	57.45 ± 15.1	57.30 ± 11.9	52.11 ± 16.3	61.32 ± 15.5	0.124
Diagnosis					**0.001**
Multinodular goiter	**14**	**28**	**25**	**24**	
Thyroid cancer	**(46.7%)**	**(90.3%)**	**(80.6%)**	**(82.8%)**	
Graves disease	**8 (26.7%)**	**1 (3.2%)**	**1 (3.2%)**	**1 (3.4%)**	
	8 (26.7%)	**2 (6.5%)**	**5**	**4**	
			(16.1%)	**(13.8%)**	
Parathyroid gland visualized					0.709
0	1 (3.4%)	-	-	1 (3.5%)	
1	1 (3.4%)	5	2 (6.5%)	4	
2	12 (41.4%)	(16.1%)	14	(14.3%)	
3		9 (29%)	(45.2%)	7 (25%)	
4	8 (27.6%)	11	9 (29%)	11	
	7 (24.1%)	(35.5%)	6 (19.4%)	(39.3%)	
		6 (19.4%)		5 (17.9%)	
Parathyroid glands removed					0.409
0	19 (63.3%)	21	27	20 (69%)	
1		(67.7%)	(87.1%)		
2	9 (30%)	9 (29%)	4 (12.9%)	7 (24.1%)	
	2 (6.7%)	1 (3.2%)	-	2 (6.9%)	
Length of stay (days)	1.77 ± 1.8	1.74 ± 1.6	1.35 ± 0.8	1.6 ± 0.9	0.603
Wound infection	1 (3.3%)	-	2 (6.5%)	1 (3.4%)	0.568
Definitive recurrent nerve paralysis	-	2 (6.5%)	-	1 (3.4%)	0.297
Postsurgical hypoparathyroidism					
Transient	10 (33.3%)	10 (32.3)	10 (32.3)	14 (48.3)	0.503
Permanent					
	1 (3.3%)	2 (6.5%)	3 (9.7%)	1 (3.6%)	0.692

patients with accidental removal of parathyroid glands had a lower median volume (Fig. 2). Similarly, it was observed that, with more glands resected in the piece, the median thyroid volume had a decreasing trend (Fig. 3). These differences did not reach statistical significance.

Discussion

Many authors have conducted studies trying to identify risk factors for complications after thyroid surgery [7, 8]. The surgery of large goiters has traditionally been considered a risk factor for postoperative complications and even appears in different scoring systems as an independent risk factor for difficult thyroidectomy with increased complications [9, 10]. It is considered that the difficulty in dissecting a larger thyroid gland or the effect that this gland may have by surrounding various structures such as the recurrent laryngeal nerve or the parathyroid glands in its growth can make its dissection more laborious and traumatic and therefore increase the incidence of complications.

Daher R and collaborators [11] described that the presence of a large goiter was a risk factor for the incidence of both transient and definitive recurrent laryngeal nerve paralysis,

Table 4 Comparison between transient and permanent hypoparathyroidism

	Transient hypoparathyroidism		*P*	Permanent hypoparathyroidism		*p*
	No ($n = 77$)	Yes ($n = 44$)		No ($n = 114$)	Yes ($n = 7$)	
Gender (female)	**66 (85.7%)**	**31 (70.4%)**	**0.043**	91(79.8%)	6 (85.7%)	0.704
Age (yo)	58.12 ± 15.6	54.97 ± 13.7	0.268	57.10 ± 14.9	54.88 ± 16.9	0.217
Diagnosis			0.647			0.885
Multinodular goiter	60 (77.9%)	31 (70.4%)		86 (75.4%)	5 (71.4%)	
Thyroid cancer	6 (7.8%)	5 (11.4%)		10 (8.8%)	1 (14.3%)	
Graves disease	11 (14.2%)	8 (18.2%)		18 (15.8%)	1 (14.3%)	
Parathyroid gland visualized			0.696			0.957
0	1 (1.3%)	1 (2.3%)			-	
1	10 (13%)	2 (4.5%)		2 (1.7%)	1 (14.3%)	
2	26 (33.7%)	16 (36.4%)		11(9.6%)	2 (28.5%)	
3	25 (32.4%)	14 (31.8%)		40 (35%)	2 (28.5%)	
4	15 (19.4%)	9 (20.4%)		37 (32.4%)	2 (28.5%)	
Parathyroid glands removed			**0.003**			**< 0.001**
0	**62 (80.5%)**	**26 (59%)**		**85 (74.6%)**	**3 (42.8%)**	
1	**15 (19.5%)**	**13 (29.5%)**		**27 (23.7%)**	**1 (14.3%)**	
2	**-**	**5 (11.3%)**		**2 (1.75%)**	**3 (42.8%)**	
Length of stay (days)	**1.14 ± 0.5**	**2.43 ± 1.8**	**< 0.001**	1.56 ± 1.2	2.57 ± 2.5	0.328
Volume (ml)	28.2 (28–43)	32 (20–61)	0.525	28.9(28–55)	29.9 (20–53)	0.982
Weight (grams)	69 (29–97)	82.8 (29–110)	0.903	73.85 (29–100)	80.7 (67–107)	0.658

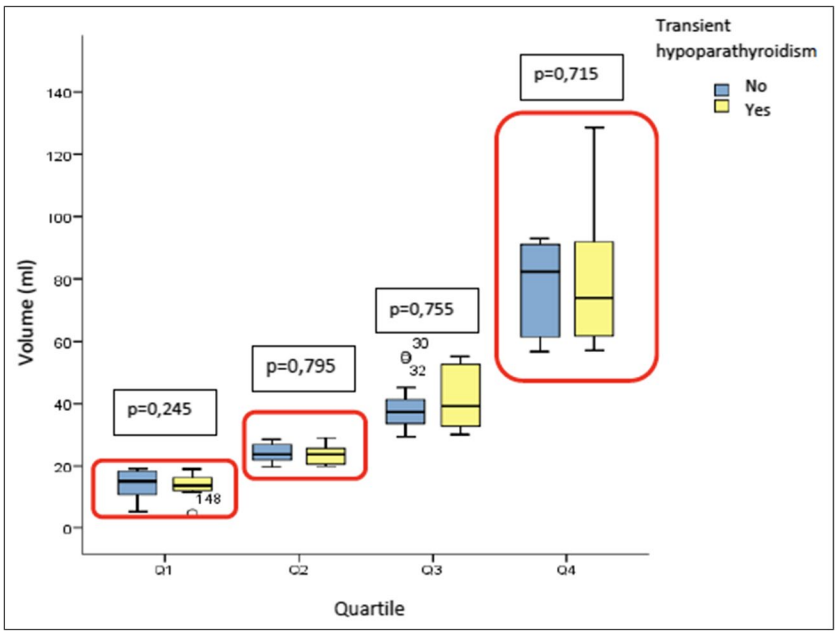

Fig. 1 Relationship between volume and post-surgical transient hypoparathyroidism

as their data showed rates more than double the total patients (4.4% vs 1.7, $p < 0.005$), justified by a more laborious dissection and identification of the nerve, mainly at the level of the Zuckerkandl tubercle. This same fact has been described in similar articles [12]. In our series, the number of definitive recurrent nerve paralysis is so low that it is difficult to draw conclusions, but only one of them occurred in the quartile of larger thyroid glands. The rest took place in surgeries of small glands. Indeed, the timing of the first vocal cord assessment is controversial. However, all patients with paralysis were evaluated until recovery or until 1 year of follow-up to assess the definitive injury rate which is much more accurate.

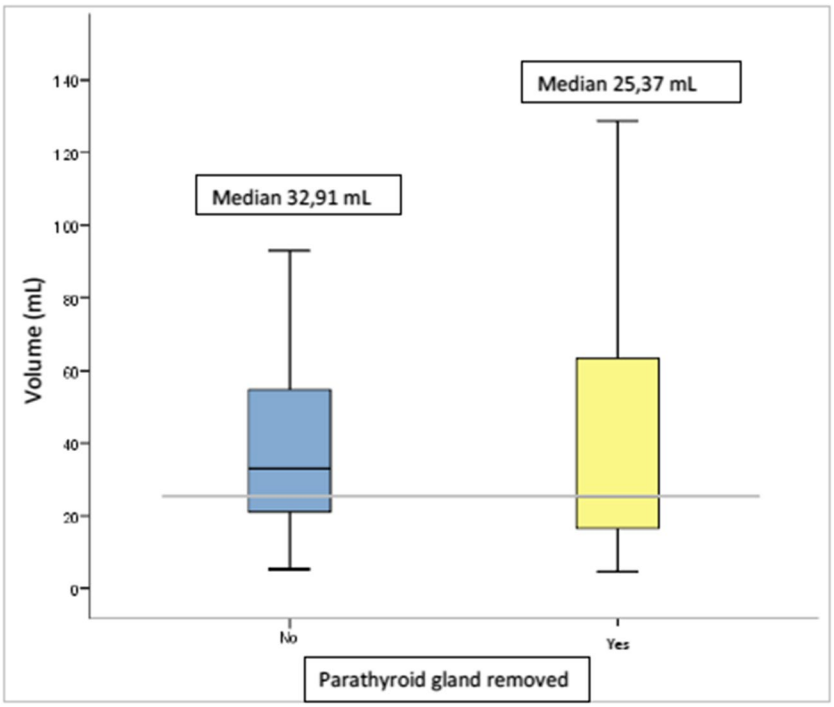

Fig. 2 Relationship between volume and removal of parathyroid glands

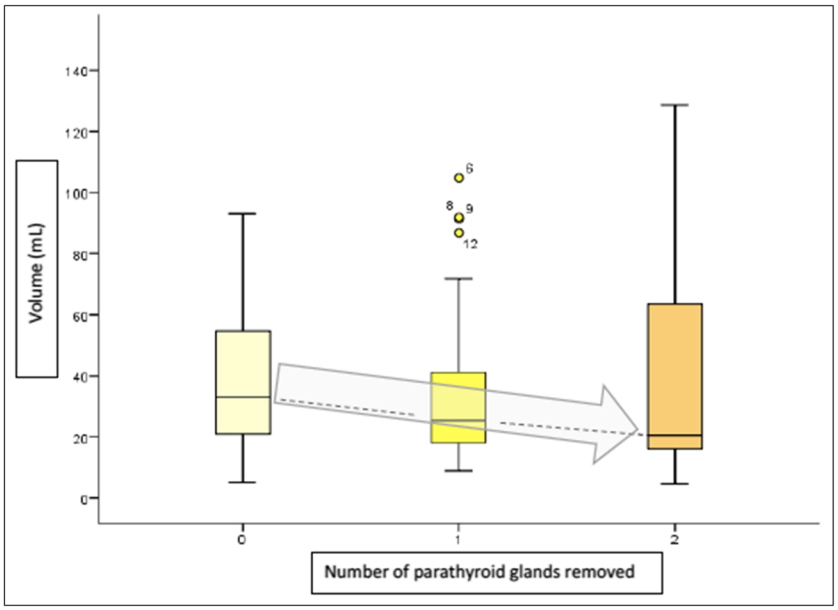

Fig. 3 Number of parathyroid glands as a function of thyroid volume

Regarding hypoparathyroidism, both temporary and permanent, due to its high incidence, it is easier to obtain conclusions. In our study, there was no difference in this postoperative complication among the different glandular size groups. There is a slight tendency towards a higher rate of temporary hypoparathyroidism in group Q4, but one of the lowest rates of permanent hypoparathyroidism, all of which is not statistically significant. When conducting a bivariate study between patients who developed or did not develop hypoparathyroidism after surgery, no risk factor was found, except for the number of parathyroid glands removed. Neither weight nor glandular volume was a risk factor. In the study by Rios A and colleagues [13], they found that both volume and weight of the glandular was an independent risk factor for the development of this complication. On the other hand, in other studies already mentioned [11],

glandular weight only influences the development of temporary hypoparathyroidism, not permanent, findings that are in line with what is described in our series. In that sense, we propose the hypothesis that a progressive growth of the thyroid gland can "displace" the parathyroid glands, which causes, although the thyroid dissection is more laborious and may have temporary vascular compromise, this displacement "protects" them from permanent damage or accidental removal. As it is not a blinded study, there is a possibility of bias that surgeons may be more careful when operating on this type of patient. In any case, before starting the study, we did a small retrospective study in which we noted that the complication rate was similar to that found in the prospective collection.

In this sense, in recent years, the importance of in situ preservation of parathyroid glands has been developed from the work of Leire and colleagues [14]. This desire for in situ preservation has been one of the reasons for the development of fluorescence devices, which are currently being evaluated in a large number of endocrine surgery units. Another very interesting finding of our study, in line with the previous hypothesis, is that (although not significantly) there is a tendency for the volume of the thyroid gland in patients in whom some parathyroid gland was removed to be smaller. Furthermore, the number of parathyroid glands increases inversely proportional to the thyroid volume (Figs. 2 and 3). This interesting finding may be the subject of future studies with a larger patient volume.

As for the last discussed complication, postoperative bleeding, there were no cases in 121 patients, so no conclusions can be drawn, although it is true that there was no incidence even in the largest goiters, significant findings.

In summary, the size of the thyroid gland has not been shown to be a risk factor for the development of postoperative complications, contrary to what has traditionally been considered. The incidence of hypoparathyroidism, recurrent injury, or bleeding is similar to that found after surgery on smaller glands if performed by a skilled surgeon and with attention to the preservation of the parathyroid glands.

Authors' contributions Joaquín Gómez-Ramírez: design, data collection, writing, and review. Paula Cubillo Heras: design, data collection, and review. Raquel Arranz Jiménez: design, data collection, and review. Luz Divina Juez Saez: design and statistic analysis. Elisa York Pineda: design and review. Camilo Zapata Syro: design and review. Constantino Fondevila Campo: review.

Declarations

Conflict of interest The authors declare no competing interests.

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