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REVIEW ARTICLE

NEUROVASCULAR ANATOMY REVIEW IN THYROID AND PARATHYROID SURGERY. SURGICAL PROCEDURE TO MINIMIZE ADVERSE EVENTS

Revisión anatómica neurovascular en cirugía tiroidea y paratiroidea. Sistemática quirúrgica para minimizar eventos adversos

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SUMMARY: Introduction and objective: Recurrent laryngeal nerve (RLN) injury is the most important complication in thyroid surgery and its side effects vary from dysphonia in unilateral laryngeal paralysis to stridor in bilateral laryngeal paralysis. Therefore, the anatomical identification and functional preservation of the nerve is essential in thyroid surgery. A variety of landmarks have been classically considered for this nerve's identification, including the inferior thyroid artery (ITA), Zuckerkandl's tubercule and Berry's and Gruber's ligaments. This study's main objective is to identify the anatomical relationship between the recurrent laryngeal nerve and the inferior thyroid artery in order to determine the surgical procedure that best avoids recurrent injury. Method: This study reviews 440 thyroidectomies performed by the same surgeon - including total thyroidectomies, hemithyroidectomies and parathyroidectomies - from September 2011 to December 2020. The relationship between the recurrent nerve's positions regarding the inferior thyroid artery was divided into prearterial, retroarterial or interarterial (between the bifurcation of branches of the artery). Other secondary variables were studied, including RLN branching, neuromonitoring, and

parathyroid gland positions and their influence on post-surgical hypoparathyroidism. In total, 695 recurrent laryngeal nerves were dissected. Results: A total of 440 patients underwent surgery. Total thyroidectomy was performed in 253, hemithyroidectomy with or without isthmectomy in 159, isolated isthmectomies in 2 and parathyroidectomies in 26 patients. A total of 695 recurrent laryngeal nerves (RLN) were dissected, 690 (99.2%) nerves were identified, being 6 of them non-recurrent right laryngeal nerves (0.8%). On the right side the predominant nerve position was prearterial (50%) and on the left side the retroarterial crossing was predominant (69%). Other variables studied were the anatomical divisions of RLN before entering the larynx, observing nerve bifurcations in 46.7% of right nerves and 29.6% of left RLN. Superior parathyroid glands were positioned in 83.7% of the cases in a high position, inferior parathyroid glands were positioned in a low position in 70% of cases. Neuromonitoring was performed in 70% of RLN and the rates of unilateral transient and permanent laryngeal paralysis were 1.2% and 0.8% respectively. Discussion: Identification and preservation of the recurrent laryngeal nerve (RLN) is paramount in thyroid surgery to prevent injury, given its variable anatomical relationship with the inferior thyroid artery (ITA). A neurovascular anatomy review is carried in a series of 440 thyroidectomies. Conclusions: The anatomical relationship between RLN and the inferior thyroid artery (ITA) is the main landmark in recurrent laryngeal nerve's surgical identification. It helps the anatomic preservation of RLN by decreasing and avoiding the feared potential nerve injuries and their subsequent complications.

KEYWORDS: recurrent laryngeal nerve; thyroidectomy; neuromonitoring.

RESUMEN: Introducción y objetivo: La lesión del nervio laríngeo recurrente (NLR) es la complicación más importante en la cirugía de tiroides y sus efectos secundarios varían desde disfonía en la parálisis laríngea unilateral hasta estridor en la parálisis laríngea bilateral. Por tanto, la identificación anatómica y preservación funcional del nervio es fundamental en la cirugía de tiroides. Clásicamente se han considerado una variedad de puntos de referencia para la identificación de este nervio, incluida la arteria tiroidea inferior (ITA), el tubérculo de Zuckerkandl y los ligamentos de Berry y Gruber. El principal objetivo de este estudio es identificar la relación anatómica entre el nervio laríngeo recurrente y la arteria tiroidea inferior para determinar el procedimiento quirúrgico que mejor evite la lesión recurrente. Método: Este estudio revisa 440 tiroidectomías realizadas por un mismo cirujano -incluyendo tiroidectomías totales, hemitiroidectomías y paratiroidectomías- desde septiembre de 2011 a diciembre de 2020. La relación entre las posiciones del nervio recurrente con respecto a la arteria tiroidea inferior se dividió en prearterial, retroarterial o interarterial (entre la bifurcación de ramas de la arteria). Se estudiaron otras variables secundarias, incluida la ramificación del NLR, la neuromonitorización y la posición de las glándulas paratiroides y su influencia en el hipoparatiroidismo posquirúrgico. En total, se diseccionaron 695 nervios laríngeos recurrentes. Resultados: Un total de 440 pacientes fueron intervenidos quirúrgicamente. Se realizó tiroidectomía total en 253, hemitiroidectomía con o sin istmectomía en 159, istmectomías aisladas en 2 y paratiroidectomías en 26 pacientes. Se diseccionaron un total de 695 nervios laríngeos recurrentes (NLR), de los que se identificaron 690 (99,2%) nervios, siendo 6 de ellos nervios laríngeos derechos no recurrentes (0,8%). En el lado derecho la posición nerviosa predominante fue prearterial (50%) y en el lado izquierdo predominó el cruce retroarterial (69%). Otras variables estudiadas fueron las divisiones anatómicas del NLR antes de ingresar a la laringe, observándose bifurcaciones nerviosas en el 46,7% de los nervios derechos y el 29,6% de los NLR izquierdos. Las glándulas paratiroides superiores se ubicaron en el 83,7% de los casos en posición alta, las glándulas paratiroides inferiores se ubicaron en posición baja en el 70% de los casos. Se realizó neuromonitorización en el 70% de los NLR y las tasas de parálisis laríngea unilateral transitoria y permanente fueron del 1,2% y 0,8% respectivamente. Discusión: La identificación y preservación del nervio laríngeo recurrente (NLR) es fundamental en la cirugía tiroidea para evitar lesiones, dada su relación anatómica variable con la arteria tiroidea inferior (ATI). Se realiza una revisión de la anatomía neurovascular en una serie de 440

tiroidectomías. Conclusiones: La relación anatómica entre el NLR y la arteria tiroidea inferior (ITA) es el principal punto de referencia en la identificación quirúrgica del nervio laríngeo recurrente. Ayuda a la preservación anatómica del NLR disminuyendo y evitando las temidas posibles lesiones nerviosas y sus posteriores complicaciones.

PALABRAS CLAVE: nervio laríngeo recurrente; tiroidectomía, neuromonitorización.

INTRODUCTION

Thyroidectomy is the most frequent surgical procedure performed within endocrine and head and neck surgery. Its surgical technique has evolved slowly over the years, with revolutionary changes during the 19th and the first half of the 20th century. Thyroid pathology was first mentioned 2700 years before Christ and Theodor Kocher is considered to be thyroid surgery's pioneer. Galen of Pergamon was the first anatomist to describe the recurrent laryngeal nerve (RLN) as a branch of a cranial nerve. Later, Vesalius and Wilis described the anatomy of laryngeal nerves and specifically the RLN. Subsequently Lahey, in 1923, emphasized the importance of a standardized technique for the identification of the RLN during thyroid surgery [1].

RLN is a mixed nerve with motor, sensory and parasympathetic branches. The motor branch innervates all of the intrinsic laryngeal muscles, except for the cricothyroid muscle which is innervated by the external branch of the superior laryngeal nerve. Before entering the larynx, the RLN branches to the cricopharynxgeus muscle and the inferior constrictor muscle [2].

The most feared complication in thyroid surgery is RLN palsy. Complications range from minor dysphonia to aspiration in unilateral palsies or even dyspnea in bilateral palsies, which is potentially life-threatening. Therefore, identification and functional preservation of RLN is essential during thyroid surgery [3].

The rate of RLN palsy ranges from 0.5 to 20% worldwide (in these surgeries specifically) The risk of recurrent laryngeal nerve injury depends on multiple factors such as thyroid pathology, surgical technique, anatomical variables and surgical experience [1-3].

Many studies have shown that identification of the RLN during thyroid surgery reduces the risk of injury and recurrent damage during dissection, hence most surgeons routinely identify the nerve during surgery. Classically, there are several anatomical structures and landmarks that help in RLN identification, such as the intersection of the nerve with the inferior thyroid artery (ITA), its course in the tracheoesophageal groove, with significant differences on the right and left side, and, if the Zuckerkandl's tubercule is present, the relationship to its position. Anatomical knowledge is of special importance, as well as its variability in the path and route of the RLN from the base of the neck to its entrance into the larynx to avoid nerve injury [4].

As previously mentioned, a fundamental anatomical structure in the recognition of RLN is the ITA (branch of the subclavian artery). Both structures are closely related and anatomically cross one-another [4].

In anatomical dissection studies, branching patterns have been observed in up to 43% of cases on both sides, divided into one or several nerve branches, and these must be taken into account. In these cases, the laryngeal motor branches are usually the anterior or internal ones. It has been reported that the distance from cricoid cartilage inferior bode to the division into one or several branches ranges from 0.5 -1 cm. [5].

RLN trajectory can be altered according to other variables such as the presence of neoplasms

that can encompass the nerve, cervical or substernal compressive goiters with risk of displacement, and even inflammatory phenomena and thyroiditis. In rare exceptions the right RLN exits directly from the vagus nerve and does not present recurrence through the right subclavian artery (< 1%). These cases can associate vascular anomalies such as the presence of a retroesophageal right subclavian artery. Classically these anatomical changes have been linked to the clinical presentation of "dysphagia lusoria". In these situations, the nerve is more vulnerable and susceptible to injury during surgery [6,7].

The entrance of the RLN in the larynx is the area where it has an intimate relationship with the thyroid gland and the thyroid suspensory ligaments (Berry and Gruber's ligaments). This area presents an important vascularization and is the place where the nerve is most easily injured either by traction, thermal damage or even nerve section [8].

The aim of the study is to analyze the relationship of the RLN with ITA during thyroid surgery, as well as to see the nerve divisions and the anatomical arrangement of the parathyroid glands, with the purpose of trying to minimize postoperative complications such as recurrent injury and hypoparathyroidism.

MATERIAL AND METHODS

A retrospective clinical study was conducted in *Hospital Clínico Universitario de Valladolid* (Department of Otolaryngology (ENT)/Head and Neck Surgery) from September 2011 to December 2020 (9 years and 3 months). Ethical authorization was obtained prior to this study's design (CEIm code 21-2296). A total of 440 patients underwent thyroidectomy by the same surgeon. The mean age was 58 years with a range between 19 and 84 years of age. The prevalence by sex was mostly female, 81.1% were women (357 patients) and the remaining 18.9% were men (83 patients). Forty-six percent had no relevant previous medical history. Hypertension was the main pathology (130 patients). 36% of the patients had a family history of thyroid cancer and only 11% had at least one of these risk factors for thyroid cancer (iodized salt deficiency, family history nd previous irradiation).

The different indications for surgical treatment in our patient sample are shown in Table 1. The most common surgical indication was bilateral euthyroid multinodular goiter with a frequency of 114 patients. The second most common causes were all tied at 12, %, being a single thyroid nodule, unilateral multinodular goiter and papillary thyroid cancer.

Table 2 shows the type of surgery performed. Total thyroidectomy was performed in 253 patients, hemithyroidectomy with or without isthmectomy in 159 patients, isolated isthmectomies in 2 patients and isolated parathyroidectomies in 26 patients. Lateral therapeutic lymph node dissections were performed in 23 patients and central selective lymph node dissections were required in 10 cases. Some radiological tests were performed before surgery: ultrasound in 62% of patients, ultrasound and computed tomography (CT) in 17%, ultrasound and scintigraphy in 12% and isolated CT in 5.8% of cases.

Table 1. Surgery indication.

	Frequency	Percentage
Thyroid nodule	56	12,7%
Unilateral MNG (Multinodular goiter)	56	12,7%
Euthyroid Bilateral MNG	114	25,9%
Toxic MNG	28	6,3%
Graves-Basedow	23	5,2%
Suspected thyroid cancer	28	6,3%
Papillary thyroid carcinoma	53	12%
Carcinoma + lymph node metastases	23	5,2%
1ºHPT (Hyperparathyroidism)	30	6,8%
2º HPT	3	0,6%
Medular carcinoma	2	0,4%
MNG + HPT	24	5,4%
Total	440	100%

(MNG= Multinodular goiter, HPT= Hyperparathyroidism)

Table 2. Type of surgery performed.

	Frequency	Percentage
Hemithyroidectomy	143	33,5%
Total Thyroidectomy	205	46,5%
Isthmectomy	2	0,4%
TT + Central neck disection	10	2,2%
TT+ Lateral neck disection	23	5,2%
Isolated parathyroidectomy	19	4,3%
Bilateral parathyroidectomy	2	0,4%
Subtotal parathyroidectomy	2	0,4%
Unilateral double parathyroidectomy	3	0,6%
TT + Parathyroidectomy	15	3,75%
Hemithyroidectomy + Parathyroidectomy	16	3,4%
Total	440	100%

(TT= Total Thyroidectomy)

All patients underwent surgery under general anaesthesia with vocal-cord-videolaryngoscopy beforehand. The standard surgical technique was extracapsular dissection (in 64% of cases the prethyroid muscles were not sectioned, in 26% a unilateral section of the muscles was performed and in 10% a bilateral section was required), performed on all patients.

The predominant hemostasis system used during these surgeries was sealed systems and bipolar coagulation (in 378 cases), associating ligation in 62 patients.

The most important surgical steps were middle thyroid vein's ligation (if present), ligation of the superior thyroid pedicle with anatomical preservation of superior laryngeal nerve's external branch (only identified in 5.2% of cases) and identification of the RLN at its intersection with the ITA.

The ITA was considered the main anatomical reference in the identification of the RLN. On both sides, the crossing between RLN and ITA was established in three patterns; prearterial, retroarterial or interarterial, as well as the presence of one or more anatomical branches of the RLN with the aim of establishing a systematic surgical approach.

Once the RLN was identified, its trajectory was followed up to its entry into the larynx and its relationship with other anatomical references. Other secondary variables were studied such as intraoperative neuromonitoring (NIM) of RLN and its influence on its paralysis (70% of the dissected RLN were neuromonitored) as well as the anatomical position of the parathyroid glands and its repercussion on post-surgical hypoparathyroidism. Three anatomical positions worked as references: the high position located at the level of the entrance of the RLN in the larynx, the middle position at the level of the intersection between RLN and the ITA and the low position located at the level of the thyrotympanic fat.

RESULTS

In the 440 patients studied, 695 nerves were dissected (365 right RLN and 330 left RLN). We were able to identify 690 RLNs (99.2%) of all the nerves studied, of which 6 right nerves were non-recurrent lower laryngeal nerves (0.8% of the total RLNs). The 5 RLNs that were not identified were due to isolated isthmectomies and selective parathyroidectomies. On the right side, the predominant relationship between the RLN and ITA was prearterial (50%), in 30,6% of these cases the nerve had an interarterial position and in 15,8% of the nerves were in a retroarterial position. The nerve was not identified in 1%.

On the left side the retro-arterial position predominated by 69%, followed by 21,8% interarterial and 8,7% prearterial position. Only 0.3% of the left RLN were not identified (Table 3). Sub-sternal goiters accounted for 23% of all thyroids operated on.

Table 3. RLN and ITA relationship.

	RIGHT		LEFT	
	Number	Frequency	Number	Frequency
Prearterial	185	50%	29	8,7%
Retroarterial	58	15,8%	228	69%
Interarterial	112	30,6%	72	21,8%
Non-recurrent	6	1,6%	0	0%
Not visualized	4	1%	1	0,3%
TOTAL	365	100%	330	100%

Another anatomical aspect studied was the division of the RLN before entry. There were no statistical differences between the sides, finding on the right side a single RLN in 52,1% of the cases, bifurcated RLN in 46,1% and trifurcated RLN in 1.6% of the cases. On the left side, the single branch also predominated with 69,9%, followed by the bifurcated nerve with 27.6% and the presence of 3 or more branches in 2.4% (Table 4). Non-recurrent nerves and those that were not identified were excluded.

The third anatomical variable studied was the position of the parathyroid glands (Table 5). The upper parathyroid glands were predominantly located in the high position in 83.7% of the cases and in the middle position in 16.20%. Nineteen percent of all upper parathyroid glands were not seen and only 0.75% were reimplanted.

On the other hand, the lower parathyroid glands were located in the middle position in 30% of the cases and 70% of them were located inferiorly, 37% of all the lower parathyroid glands were not identified and only 2.2% of them were reimplanted.

Another variable analyzed was neuromonitoring (Table 6). Of the 440 patients operated on, 307 (70%) were neuromonitored. In the post-surgical laryngoscopy of the neuromonitored patients, 87.6% were true negatives (positive recordings without laryngeal paralysis), 9,4% false positives (negative recordings without laryngeal paralysis) and 2,9% true positives (negative recordings with unilateral laryngeal paralysis) (Table 7). In the 695 operated nerves there were 9 unilateral temporal palsies (1.2%) and 6 unilateral definite palsies (0.8%). Seventy-five percent of the temporary and 80% of the definitive palsies occurred with neuromonitoring. Of all the definitive paralyses, 4 were due to oncological pathology and one was a parathyroidectomy.

Table 4. RLN branches.

	RIGHT		LEFT	
	Number	Frequency	Number	Frequency
Single branch	185	52,1%	230	69,9%
Bifurcated	164	46,1%	91	27,6%
Three or more branches	6	1,6%	8	2,4%
TOTAL	355	100%	329	100%

Table 5. Position of the parathyroid glands.

	Upper/Superior	Lower/Inferior
High	83,7%	0%
Medium	16,2%	30%
Low	0%	70%

Table 6. Neuromonitoring.

	Frequency	Percentage
No	133	30%
Yes	307	70%
Total	440	100%

Table 7. Neuromonitoring / laryngoscopy.

	Frequency	Porcentage
TN (+ register / No paralysis)	269	87,6%
TP (- register / Unilateral Paralysis)	9	2,9%
FP (- register / No paralysis)	29	9,4%
FN (+ register / Paralysis)	0	0%
Total	307	100%

(TN: true negative; TP: true positive; FP: fake positive; FN: fake negative)

DISCUSSION

Identification and preservation of the recurrent laryngeal nerve is essential in thyroid surgery. For this purpose, anatomical knowledge of the nerve and its possible anatomical variants is essential in order to avoid injury during its dissection. The ideal way to avoid injury to RLN is to identify it and follow its recurrence during thyroid dissection carefully, since the risk of permanent nerve injury ranges between 1-10% [8]. In 1970, Riddel reported that thyroidectomy is a precise surgery and compared post-thyroidectomy laryngeal paralysis to post-surgical facial paralysis. Therefore, the

main problem during thyroid surgery is laryngeal paralysis and a surgical knowledge of cervical neurovascular anatomy is required [9]. Although still somewhat controversial, identification of the RLN is proposed as the initial step in a thyroidectomy and according to our model it's the only method to avoid injury to the RLN.

The first and most important landmark for RLN anatomical identification is the inferior thyroid artery (ITA). However, it can be difficult to identify due to the neurovascular anatomical variants and the pathological characteristics of the gland. It is not unusual for the nerve to cross the artery, either anteriorly (prearterial), posteriorly (retroarterial) or between the arterial branches (interarterial). However, the anatomical relationship between these two structures is not consistent on both sides [1].

The easiest place to injure the nerve is at the level of Berry's ligament, hence identification of the nerve in this area is risky. The most common injuries are usually tractions, thermal injuries and, less frequently, sections.

In our study we observed that a retroarterial relationship was the most frequent with a total of 286 nerves (41.1%). Prearterial crossing between RLN and ITA on both sides occurred in 214 nerves (30.7%). The interarterial nerve position was the least common, in 184 dissected nerves (26,4%).

On the right side the prearterial position predominated, being visualized in 185 nerves (50%), the interarterial position was observed in 112 nerves (30,6%) and the retroarterial position was found in 58 nerves (15,8%). On the left side the predominant nerve position was retroarterial, observed in 228 nerves (69%), the interarterial position was seen in 72 cases (21,8%) and anterior to the ITA in 29 patients (8,7%). Studies by Saldanha et al and Ardito et al observed that the most frequent relationship was retroarterial with 89% and 61% of cases respectively [1, 9]. Hisham and Lukman also observed the same relationship with a frequency of the retroarterial variant of 83.8% [10]. In contrast, the review by Sturniolo et al provided data contrary to the majority of studies, with the retroarterial variant with percentages of 22% and 36% on the right and left sides, respectively [11].

In our study the most frequent position was retroarterial, however, not with such a high frequency, probably because the interarterial position is considered as a retroarterial variant in the aforementioned reviews. In most studies, as mentioned above, the most frequent relationship was retroarterial, especially on the left side.

On the other hand, with the aim of minimizing recurrent nerve lesions, the branching of RLN before entering the larynx was studied and it was observed that on the right side the nerve was single in 185 cases (52,1%), bifurcated in 164 cases (46,1%) and presented 3 or more branches in 6 cases (1.6%). On the left side it was observed that 230 nerves had a single trunk (69,9%), 91 nerves were bifurcated (27,6%) and 8 nerves had 3 branches (2.4%). There are few studies where the branches of RLN are observed before entering the larynx [1, 10], nevertheless, it is fundamental to identify if it is a single trunk or if it presents more branches since in this latter case the main laryngeal motor branch is the internal one being the external divisions esophageal motor branches.

In addition to the surgical experience in order to identify the divisions, neuromonitoring is very useful in these cases since the internal branch presents nerve signal and the external branch usually gives a weak or no signal. In our study we observed that the single nerve was predominant on both sides, perhaps with a higher prevalence on the left side (69,9%).

It is not uncommon to find the nerve at the level of the junction with the artery or inferior to it and it is usually recommended to ligate the ITA as close as possible to the thyroid capsule to avoid nerve injury. If this is not possible, it must be identified in the superior region close to the entrance and Berry's ligament, the area where it is most easily injured.

In concurrence with the medical literature, we observed the left nerve having a vertical trajectory

in the tracheoesophageal groove and the right nerve having a more oblique trajectory in all of our dissections.

In their review, Hunt et al found the RLN in the tracheoesophageal groove on the right and left side in 65% and 77% of cases respectively. Therefore, the tracheoesophageal groove can also be considered an anatomical landmark in this nerve's identification [8].

CONCLUSIONS

According to the medical literature, many safe surgical techniques have been described for the identification of RLN in order to decrease the rates of laryngeal paralysis. The main anatomical landmark is the crossing of the RLN with the ITA. Other landmarks to take into consideration are Zuckerkandl's tubercle, Berry's ligament or the tracheoesophageal groove. In-depth knowledge of the cervical neurovascular anatomy and its possible variants is essential in order to try to ensure the anatomical and functional integrity of the RLN. In our study we concluded that the relationship of the RLN to the ATI is a safe and consistent landmark in thyroid surgery and its identification should be a standard technique to try to avoid and minimize laryngeal paralysis.

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