

Mexican Association of General Surgery, A.C. Enhanced Surgical Recovery Program. Thyroid endocrine surgery

*Asociación Mexicana de Cirugía General, A.C.
Programa de Recuperación Quirúrgica Mejorada.
Cirugía endocrina tiroidea*

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ABSTRACT

The main objective of enhanced recovery programs in surgery is to provide an efficient treatment based on the best scientific evidence in order to shorten the postoperative recovery time of patients, reduce the incidence of complications inherent to hospitalization and surgical treatment, and consequently reduce hospital costs. In our country, more than 50% of thyroidectomies are performed by low-volume surgeons, which has already been shown to increase the possibility of post-surgical complications, such as hypoparathyroidism and transient or permanent chordal paralysis. In the understanding that achieving the availability of high volume surgical human resources throughout the national territory is not a viable short-term objective, despite the efforts to train high specialists in endocrine surgery, one of the initiatives of the Mexican Association of General Surgery, A.C., is to issue a series of recommendations that support national surgeons to have better surgical results, with the sole objective of increasing the quality of care of the Mexican population. Until now, there was no established protocol in Mexico for

RESUMEN

Los programas de recuperación mejorada en cirugía tienen como principal objetivo brindar un tratamiento eficiente basado en la mejor evidencia científica con la finalidad de acortar el tiempo de recuperación postoperatoria de los pacientes, disminuir la incidencia de complicaciones inherentes a la hospitalización y tratamiento quirúrgico; y por consecuencia reducir los costos hospitalarios. En nuestro país, más de 50% de las tiroidectomías son realizadas por cirujanos de bajo volumen, lo que ya se ha demostrado que incrementa la posibilidad de complicaciones postquirúrgicas, tales como hipoparatiroidismo y parálisis cordal transitoria o permanente. En el entendimiento de que alcanzar la disponibilidad de recursos humanos quirúrgicos de alto volumen en todo el territorio nacional es un objetivo no viable a corto plazo, a pesar de los esfuerzos de formar altos especialistas en cirugía endocrina, una de las iniciativas de la asociación mexicana de cirugía general, A.C., es la de emitir una serie de recomendaciones que apoyen a los cirujanos nacionales a tener mejores resultados quirúrgicos, con el objetivo único de incrementar la



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patients undergoing thyroid surgery. The purpose of the present work was to make a consensus of experts to issue recommendations in the preoperative, intraoperative and postoperative period to improve the outcomes of patients undergoing thyroidectomy. All these recommendations are based on the best available scientific evidence and are oriented to surgeons of both high and low surgical volume in terms of thyroidectomy.

calidad de atención de la población mexicana. Hasta la fecha actual, en México no existía, un protocolo establecido para los pacientes que son intervenidos de cirugía tiroidea. El presente trabajo tuvo como finalidad realizar un consenso de expertos para emitir recomendaciones en el periodo preoperatorio, intraoperatorio y postoperatorio para mejorar los desenlaces de los pacientes intervenidos de tiroidectomía. Todas estas recomendaciones basadas en la mejor evidencia científica disponible y orientadas a cirujanos tanto de alto como de bajo volumen quirúrgico en cuanto a tiroidectomía se refiere.

INTRODUCTION

Thyroid pathology, especially structural pathologies such as thyroid nodules, has a prevalence of approximately 25% in the general population, followed in order of frequency by functional pathologies such as hypothyroidism and hyperthyroidism (especially those of autoimmune etiology).¹ All these pathologies are of potential surgical treatment and, therefore, of interest to the general surgeon and the subspecialist. In addition to this, the procedures associated with endocrine pathology most frequently performed at the specialty and high specialty level are those related to the thyroid gland, especially with thyroid malignant disease, which is the third leading cause of oncologic surgery in our country according to data reported by Globocan.^{2,3} In such a way that the work carried out by Table 4 (endocrine surgery) within the National Surgeon's Meeting (ENC) of 2021 for the Mexican Enhanced Surgical Recovery Program (PRQ-MX) of the Mexican Association of General Surgery (AMCG) has focused on thyroidectomy patients.

The primary objective of AMCG's PRQ-MX is to achieve efficient and quality recovery in surgical patients through cost-effective pre-, intra-, and postoperative interventions based on the best scientific evidence published to date. The impact of these measures not only crystallizes in the reduction of potential postoperative complications in patients but also in the length of hospital stay, as well as in the costs for the patient and the health system.⁴

With this scenario and these objectives in mind, the activities of roundtable 4 for

the ENC began with elaborating a series of recommendations classified under the GRADE schemes for the level of evidence and degree of recommendation. These recommendations were initially submitted for review in two independent sessions in virtual surveys using the SurveyMonkey® tool sent electronically to structure a definitive list of guidelines to be discussed and voted on during the virtual activities of the ENC 2021. During the ENC, these guidelines were reviewed, modified, and approved by consensus through the Delphi method, establishing a majority consensus among the participating experts of at least 70%. The final product of months of work in table 4 concerning the PRQ-MX in thyroid surgery are summarized in [Table 1](#) and [Figure 1](#) and are analyzed in detail below according to the perioperative moment.^{5,6}

PREOPERATIVE TIME

What is the minimum recommended approach for appropriate surgical planning in patients with thyroid pathology of potential surgical treatment?

Recommendation 1. *The patient should have imaging studies and BAAD (Thin Needle Aspiration Biopsy) to determine the nature and staging of the thyroid lesion and suspicious adenopathies (high level of evidence; strong grade of recommendation).*


Cervical ultrasound (US) is the imaging study of choice in the approach to structural alterations of the thyroid gland. US evaluation in patients with thyroid pathology should

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Table 1: Summary of the recommendations described according to their level of evidence and grade of recommendation.

Preoperative	Level of evidence	Grade of recommendation
Recommendation 1. The patient should have imaging studies and BAAD (fine needle aspiration biopsy) to determine the nature and staging of the thyroid lesion and suspicious adenopathies	High	Strong
Recommendation 2. Thyroid function status should always be checked. Ideally, all patients should be admitted to surgery euthyroid. In the case of hypofunction, it should be previously replaced. In the case of hyperthyroidism, optimal pharmacological treatment should be implemented (e.g., beta-blockers, methimazole, propylthiouracil, and Lugol, as the case may be) and cardiovascular risk should be evaluated	High	Strong
Recommendation 3. Subjective voice evaluation (<i>Voice Handicap Index</i> questionnaire) is recommended. Objective evaluation by laryngoscopy or translingual ultrasound should be performed in patients with dysphonia, dysphagia, previous surgery, or imaging suspicion of recurrent laryngeal nerve invasion	Moderate-high	Intermediate
Recommendation 4. Routine assessment of 25-OH vitamin D levels and replenishment of vitamin D, if necessary, is recommended to reduce the incidence of transient post-thyroidectomy hypocalcemia	Moderate	Intermediate
Intraoperative		
Recommendation 5. The extent of thyroid resection should be adjusted to the ATA risk group and data on local invasion and lymph node metastasis	Moderate-high	Strong
Recommendation 6. Identifying and preserving the recurrent laryngeal nerves, superior laryngeal nerves, and parathyroid glands without compromising their integrity is recommended whenever possible	High	Strong
Recommendation 7. The use of advanced energy equipment (ultrasonic, advanced bipolar, mixed) is recommended to reduce blood loss and surgical time	Moderate-high	Strong
Recommendation 8. Intraoperative neuromonitoring is recommended since it has proven to be helpful in the functional preservation of the recurrent laryngeal nerve and the external branch of the superior laryngeal nerve in neck reoperations or cases of high risk for chordal dysfunction	Moderate-high	Intermediate
Recommendation 9. Routine use of drains in thyroid surgery is not recommended	High	Strong
Postoperative		
Recommendation 10. Measuring serum calcium (ionized or corrected) and PTH in the immediate postoperative period is recommended. Immediate oral use of calcium with or without calcitriol can be implemented in those patients at higher risk of hypocalcemia	High	Strong
Recommendation 11. Measurement of serum magnesium levels and its replacement, if necessary, is recommended	Low	Weak
Recommendation 12. It is recommended that levothyroxine be started immediately postoperatively in patients with total thyroidectomy or pre-existing hypothyroidism. TSH levels should be monitored in the following 4-6 weeks to adjust this substitution scheme	High	Strong

PRQ-MX THYROID SURGERY Checklist



	No.	Recommendation	Revised
Preoperative	1	Imaging studies and BAAD are available to determine the nature and staging of the thyroid lesion and suspicious adenopathies	<input type="checkbox"/>
	2	Thyroid function and vitamin D tests are normal	<input type="checkbox"/>
	3	In case of dysphonia, dysphagia, previous surgery or imaging suspicion of NUR invasion, an evaluation of chordal mobility and voice has been performed	<input type="checkbox"/>
Intraoperative	4	The extent of thyroid resection will be adjusted to the ATA risk group as well as by data on local invasion and lymph node metastasis	<input type="checkbox"/>
	5	The NUR , RENUS and parathyroid glands were preserved without compromising their integrity and function	<input type="checkbox"/>
	6	Advanced energy (ultrasound, bipolar or mixed) was used	<input type="checkbox"/>
	7	In the case of neck reoperation or high risk for chordal dysfunction, neuro monitoring was used to corroborate functional preservation of the NUR and RENUS	<input type="checkbox"/>
	8	Routine use of drains without clear indication was avoided	<input type="checkbox"/>
Postoperative	9	Serum calcium and magnesium levels were measured	<input type="checkbox"/>
	10	In case of hypocalcemia, PTH levels were measured	<input type="checkbox"/>
	11	Levothyroxine administration was initiated in patients with total thyroidectomy or pre-existing hypothyroidism	<input type="checkbox"/>
	12	TSH levels will be monitored over the next 4-8 weeks to adjust levothyroxine replacement according to the ATA risk group	<input type="checkbox"/>

PTH = parathyroid hormone. TSH = thyroid-stimulating hormone. ATA = American Thyroid Association.

Figure 1:

Quick checklist of suggested recommendations.

include at least the following: characteristics of the thyroid tissue, size of the gland, size of the nodules (in all three dimensions), location of the nodule within the parenchyma, characteristics of the nodules (composition, echogenicity, margins, presence or absence of calcifications (micro or macro), vascularity and relation between height and width of the nodule), in addition to the presence or absence of cervical lymphadenopathy suspicious of malignancy in the central (levels

VI and VII) and lateral (cervical levels II to V) lymph node compartments bilaterally. In patients with suspected locally advanced malignant thyroid disease (invasion to adjacent structures), the use of studies such as contrast-enhanced computed tomography and nuclear magnetic resonance have an added value in the preoperative planning of surgical resection, especially in patients with advanced local invasion, as well as pulmonary and distant metastases.⁷⁻⁹

The BAAD of thyroid nodules should be performed following the guidelines established by the American Thyroid Association (ATA) or by the American College of Radiology (TI-RADS stratification) concerning US stratification, as well as the Bethesda cytopathological classification for the risk of malignancy of the suspected thyroid nodule. About lymphadenopathies, BAAD should be performed (with the respective cytopathological analysis, as well as thyroglobulin measurement in the aspirate lavage) in those whose positive result for metastases could modify the degree or extent of surgical resection, especially when central compartment dissection or functional modified radical dissection is indicated.^{8,10}

Recommendation 2. *Thyroid function status should always be checked. Ideally, all patients should be admitted to surgery euthyroid. In the case of hypofunction, it should be previously replaced. In case of hyperthyroidism, optimal pharmacological treatment should be implemented (e.g., beta-blockers, methimazole, propylthiouracil, and Lugol, as appropriate), and cardiovascular risk should be assessed (high level of evidence; strong grade of recommendation).*

Dysthyroid states (hypo- or hyperthyroidism) confer an increased cardiovascular risk to the anesthetic event during surgery. In cases of patients with hyperthyroidism requiring surgical treatment, the drugs used during anesthesia, the stress of the surgical event, and even the manipulation of the gland during surgery can induce a state of thyrotoxicosis with subsequent systemic and cardiovascular repercussions in the patient. In the latter group of patients, cardiac output is increased by 50 to 300% due to sodium and water retention due to overactivation of the renin-angiotensin-aldosterone system, a fall in peripheral vascular resistance, and a positive inotropic and chronotropic effect on the myocardium. In addition, there is an increased risk for the development of atrial fibrillation in these patients, ranging from 10 to 15%. On the other

hand, hypothyroidism increases the risk of coronary events by increasing blood lipid levels, prolonging the half-life of coagulation factors, and inducing anemia. Additionally, it predisposes to the development of cardiac arrhythmias such as “torsade de pointes” or polymorphic ventricular tachycardia, decreases cardiac output by 30 to 50%, and increases peripheral vascular resistance, which puts the patient’s cardiovascular status at risk during the anesthetic event.

Because of all these effects on the cardiovascular system, which expose the patient to complications associated with the surgical event, patients who undergo thyroidectomy should be adequately assessed for anesthetic-surgical risk and myocardial function, as well as their thyroid functional status before the surgical event. Whenever possible, these patients should be biochemically and clinically euthyroid before the scheduled surgery, especially if thyroid surgery is involved.¹¹⁻²⁰

In which patients is voice evaluation recommended before thyroid surgery?

Recommendation 3. *Subjective voice evaluation (Voice Handicap Index questionnaire) is recommended for all patients undergoing thyroid surgery. Objective evaluation by laryngoscopy or trans laryngeal ultrasound should be performed in patients who report dysphonia, dysphagia, previous surgery or in whom there is suspicion of invasion of the recurrent laryngeal nerve by imaging (moderate-high level of evidence; intermediate grade of recommendation).*

Up to 33% of patients undergoing thyroid surgery may present with asymptomatic or subclinical chordal paralysis. Because of this non-negligible percentage, routine preoperative voice evaluation is recommended for all patients undergoing thyroidectomy. In addition, this evaluation provides a baseline measurement against which to compare postoperatively. Such periodic evaluation should include targeted questioning to detect changes in the quality and quality of the patient’s voice and standardized

questionnaires such as the Voice Handicap Index (VHI). In those cases, in which alterations are detected in the subjective evaluation, in patients with suspected invasion by imaging studies or who have previously undergone surgery (1.5 to 30% of these patients may present chordal palsy), an additional evaluation of the voice should be implemented with the use of tools such as transoperative ultrasound, laryngoscopy, and other validated instruments.²¹⁻²⁴

What preoperative measures impact the incidence of postoperative hypocalcemia in patients undergoing thyroid surgery?

Recommendation 4. *Routine assessment of vitamin D levels and vitamin D replacement, if necessary, is recommended to reduce the incidence of transient symptomatic post-thyroidectomy hypocalcemia (moderate level of evidence; intermediate grade of recommendation).*

The concomitant use of oral vitamin D and calcium in the immediate postoperative period of thyroidectomy patients helps avoid symptomatic hypocalcemia. It reduces the time of use of intravenous calcium preparations. On the other hand, a recent meta-analysis and systematic review found vitamin D deficiency to be a risk factor for transient post-surgical hypocalcemia and permanent hypocalcemia in cases of severe deficiency.²⁵ Furthermore, sufficient evidence exists regarding the superiority of the concomitant use of these two drugs in the prevention of postoperative hypocalcemia compared to their separate or individual use.^{26,27} Preoperative vitamin D supplementation, however, remains controversial. In 2019, Rowe et al. reported a double-blind controlled clinical trial in 150 patients at high risk for postoperative hypocalcemia (cancer, Graves' disease, and goiters) who were randomized to receive high-dose vitamin D (300,000 IU) or placebo. In this study, no significant differences were identified between the two groups regarding the primary outcome (postoperative hypocalcemia) at seven days,

21/72 (29%) in the group that received the intervention and 30/78 (38%) of those assigned to placebo ($p = 0.23$). In addition, no significant differences were found in in-hospital or symptomatic hypocalcemia events.²⁸ Conversely, Khatiwada and associates recently conducted a systematic literature review. They found nine studies (two of them placebo-controlled) in which treatments with hypercalcemic drugs (vitamin D, oral calcium, and calcium-sparing diuretics) were implemented preoperatively to avoid post-thyroidectomy hypocalcemia. In seven of the nine studies, benefits were identified in terms of reduction in the rate of post-surgical hypocalcemia in the groups that implemented these measures. Within the studies discussed, two used vitamin D exclusively, one implemented oral calcium alone, three combined oral calcium and vitamin D, and one used all three strategies (oral calcium, vitamin D, and diuretic).²⁹ In 2019, Bhetanni and colleagues reported their randomized clinical trial in 102 patients undergoing thyroidectomy surgery who were assigned a substitution schedule with vitamin D (200,000 single-dose units) + 700 mg of oral calcium carbonate or calcium alone in the preoperative period. In their study, the authors report a significant difference in the event rates of asymptomatic hypocalcemia, latent hypocalcemia (absence of symptoms with presence of Chvostek and Trousseau signs), and symptomatic hypocalcemia.³⁰ In 2020, Ramouz and his group reported their clinical trial conducted in 100 patients undergoing total thyroidectomy with preoperative documented vitamin D deficiency. They were randomized to receive placebo or replacement with 50,000 units of vitamin D3 weekly for four weeks. In their study they found a lower incidence rate of symptomatic hypocalcemia, as well as lower intravenous calcium requirements for the treatment of those patients who developed symptomatic hypocalcemia.³¹

Although more randomized, controlled clinical trials are needed, the benefit of preoperative vitamin D use to reduce the incidence of postoperative hypocalcemia outweighs the risks.

INTRAOPERATIVE TIME

What is the appropriate extent of surgical resection for patients diagnosed with well-differentiated thyroid cancer?

Recommendation 5. *The extent of thyroid surgical resection should be adjusted to the dynamic risk group of TAA, as well as data on local invasion and nodal metastasis (moderate-high level of evidence; strong grade of recommendation).*

One of the most controversial topics in thyroid surgery is the extent of surgical resection necessary for the treatment of well-differentiated thyroid cancer. In the most recent version of the 2015 American Thyroid Association (ATA) guidelines for treating thyroid nodules and well-differentiated thyroid cancer, a modification was made to the extent of resection for lesions larger than 1 cm. The previous guidelines proposed total thyroidectomies for all lesions larger than 1 cm. However, in 2015, this recommendation changed, suggesting lobectomy as an appropriate treatment for low-risk lesions of 1 to 4 cm (absence of extrathyroidal extension, lack of lymph node, or distant metastases) in patients with papillary or follicular thyroid cancer. Leaving total thyroidectomy for the treatment of high-risk lesions (such as histotype or genotype), tumors > 4 cm, or patients requiring close follow-up, adjuvant therapy with radio-iodine ablation or if so, decided by the patient following a risk-benefit discussion between the patient and the treating physician.^{32,33}

For patients with medullary or oncocytic Hürthle cell carcinoma of the thyroid, the extent of surgical resection of thyroid tissue is total thyroidectomy in all cases, except in palliative instances where the risk of complications exceeds the benefit to the patient.⁸

Cases of patients with anaplastic or undifferentiated thyroid carcinoma should undergo preoperative evaluation and multidisciplinary discussion before surgical treatment is offered. Total thyroidectomy is reserved for patients with stage IVA and IVB tumors of this type, in which an

R0 resection can be achieved without leading to complications that postpone the administration of adjuvant therapy (radiotherapy and chemotherapy). In stage IVC, the role of surgery is limited.³⁴

What intraoperative maneuvers are essential to reduce the risk of postoperative complications in patients undergoing thyroidectomy?

Recommendation 6. *Whenever possible, identification and preservation of the recurrent laryngeal nerves (RLN), external branches of the superior laryngeal nerves (ULN), and parathyroid glands, without compromising their integrity, is recommended (high level of evidence; strong recommendation).*

Chordal palsy and post-surgical hypoparathyroidism are the two complications secondary to thyroidectomy, with the most significant impact on the quality of life of patients. To avoid these complications permanently, identifying and preserving the recurrent laryngeal nerve (RLN), the external branch of the superior laryngeal nerve (ENLN), and parathyroid glands is a priority during the surgical procedure. Despite the advent of technology to avoid these complications (e.g., intraoperative neuromonitoring, parathyroid fluorescence, etc.), today's standard of care is visual identification and anatomic preservation of the structures. The most crucial preventive maneuver for post-surgical hypoparathyroidism is in situ preservation of the parathyroid glands and their vascularity.³⁵ On the other hand, although it is a recommended practice, there is controversy on the usefulness of autotransplantation of de-vascularized parathyroid glands in postoperative total thyroidectomy patients to prevent postoperative hypocalcemia.^{36,37} Likewise, the identification of the NLR reduces the risk of transection and dysfunction of the same, which is why it is the general recommendation during thyroidectomy.³⁸ In the particular case of the NLRNLS, its identification within the inter-cricothyroid space (Reeve's space or avascular plane between the upper pole of the thyroid lobe and the cricothyroid muscle)

is recommended. In case the identification of the latter is not achieved, to reduce the risk of injury, dissection as close as possible to the superior pole of the thyroid and individual ligation of the vascular structures is recommended.

How useful is the use of advanced energy devices in thyroid surgery?

Recommendation 7. *The use of advanced energy equipment (ultrasonic, advanced bipolar, mixed) is recommended to reduce blood loss and surgical time (moderate-high level of evidence; strong grade of recommendation).*

Although they are not indispensable instruments for performing thyroid surgery, current systematic reviews and meta-analyses have shown a statistically significant difference in clinical impact in favor of the use of advanced energy instruments (ultrasonic, advanced bipolar, or mixed devices) in thyroid surgery compared to the conventional technique (clamp, suture and cut plus electrocautery or monopolar energy) in terms of operative time (average difference between 20 and 22 minutes) and blood loss (20 ml).^{39,40} The same studies have shown similar rates of complications associated with the procedure. On the other hand, some meta-analyses have found a shorter operative time (8 min) in favor of using ultrasonic energy.⁴¹ However, none of the advanced energy devices are significantly superior to the other (e.g., ultrasonic vs. bipolar) in terms of operative time, blood loss or complication rates.^{42,43}

What is the clinical impact of the use of intraoperative neuromonitoring (NMio) of the recurrent laryngeal nerve (RLN) and external branch of the superior laryngeal nerve (RENLS) in thyroid surgery, and in which patients is its implementation recommended?

Recommendation 8. *The use of intraoperative neuromonitoring (IMN) in thyroid surgery is recommended since it has proven to be helpful in the functional preservation of the recurrent laryngeal nerve (RLN) and the*

external branch of the superior laryngeal nerve (ENLN), mainly in neck reoperations or patients at high risk of chordal dysfunction (**moderate-high level of evidence; intermediate grade of recommendation**).

One of the most feared complications during thyroidectomy is chordal palsy due to NLR and RENLS involvement. Intraoperative NMio is an adjuvant tool in thyroid surgery, allowing the functional evaluation of the NLR and RENLS through an intraoperative electromyographic recording. However, according to the most recently published scientific literature, the use of NMio has not been shown to be superior or inferior to anatomical identification of the LNR in relation to the outcome of transient or permanent chordal palsy.⁴⁴ Contradictorily, in the meta-analysis by Yang et al, these authors found statistically significant utility of NMio in reducing rates of transient chordal palsy.⁴⁵ In 2017, Wong and colleagues performed a systematic review and meta-analysis on the use of NMio in patients with high-risk thyroidectomy for chordal palsy (defined as reoperations, thyroid cancer, substernal or retrosternal goiter, and thyrotoxicosis). These authors found a reduction in the rates of transient and permanent paralysis in reoperations and transient paralysis in patients with thyroid cancer, recommending its use in patients at high risk for chordal palsy.⁴⁶ Finally, NMio seems to have an important role in the transoperative detection of chordal palsy, allowing the change of strategy in the transoperative period with respect to whether or not to perform complementary hemithyroidectomy at the same time in case a total thyroidectomy is necessary. With this, NMio seems to significantly reduce the incidence of cases with bilateral chordal palsy and even the need for tracheostomy.⁴⁷

What is the benefit of placing drains in patients who have undergone thyroid surgery?

Recommendation 9. *Routine use of drains in thyroid surgery is not recommended (high level of evidence; strong grade of recommendation).*

The placement of drains in thyroidectomy has been implemented in past decades with the apparent objective of decreasing the rates of postoperative cervical hematoma and seroma, as well as of reoperation in the case of the former. However, the most recent meta-analysis of the Cochrane Library, performed by Samraj et al. (analysis of 13 studies), found no significant differences in the need for reoperation, respiratory distress, surgical site infection, and low-volume seroma. On the contrary, the use of post-thyroidectomy drainage was associated with a more significant number of patients with postoperative pain, greater pain intensity, and longer hospital stays. It is important to comment that the studies in this meta-analysis did not include patients with goiters with retrosternal extension, patients at high risk of bleeding, or concomitant lateral cervical dissections.⁴⁸ Similar to what was reported by previous authors, in 2020, Soh and his group, in a meta-analysis that included 16 studies, reported a statistically significant association between the presence of cervical drainage and the development of post-surgical hematomas, as well as surgical site infection and even a more extended hospital stay.⁴⁹

Although the evidence against the routine use of active drains in thyroid surgery is clear, in special cases such as goiters with retrosternal extension or lateral modified radical dissections or extensive dissections, the use of active drains is always at the surgeon's discretion, with the only recommendation being to avoid the use of open or passive drains.

POSTOPERATIVE TIME

When and how is the risk assessment of postoperative hypocalcemia in thyroid surgery patients performed?

Recommendation 10. *To evaluate the risk of hypocalcemia in patients who have undergone thyroid surgery, it is recommended to measure serum calcium (ionized or corrected) and/or PTH in the immediate postoperative period. Immediate oral use of calcium with or without calcitriol can be implemented in those patients at increased risk of developing*

hypocalcemia (high level of evidence; strong grade of recommendation).

Postoperative transient hypocalcemia is the most frequent complication after thyroidectomy, with an estimated incidence between 19 and 38%, depending on the series analyzed.⁵⁰ Calcium measurement as a diagnosis of hypocalcemia is reliable only between 48 and 72 hours postoperatively, which prolongs the in-hospital follow-up of these patients to identify this complication.⁵¹ A recent meta-analysis and systematic review published in 2014 identified that ionized calcium levels below 0.95 mmol/L within the first 24 hours had a sensitivity between 19 and 90% for identifying postoperative transient hypocalcemia.⁵² Two other studies regarding isolated serum calcium determinations identified cutoff points of 8.4 and 7.52 mg/dL in the first 24 hours postoperatively as predictors of postoperative transient hypocalcemia.^{53,54}

On the other hand, a 2.3% decrease in preoperative serum calcium levels at 24 hours postoperatively was predictive of transient hypocalcemia in 94% of patients (sensitivity).⁵⁵ Other authors have analyzed the trend of calcium levels in two serial postoperative determinations within the first 24 hours (at 6 and 24 hours), identifying that a positive direction, that is, an increase in calcium levels between one determination and another, allows excluding a postoperative transient hypocalcemia event with a negative predictive value of 86 to 100%. Likewise, a negative trend, i.e., a decrease in calcium levels between both measurements, has a positive predictive value of 20 to 46% for postoperative transient hypocalcemia.⁵⁶ Thus, serum calcium measurements 48 to 72 hours postoperatively help predict the development of hypocalcemia. In measurements performed in the first 24 hours, the trend between two determinations (six and 24 hours) can help identify patients at risk of this complication.

Parathyroid hormone (PTH) has a plasma half-life of three to four minutes, so some authors have attempted to identify the predictive utility of postoperative PTH levels and the risk of developing hypocalcemia after thyroidectomy. In 2017, Mathur et al. published a systematic review

regarding postoperative PTH determination and post-thyroidectomy hypocalcemia. These authors identified a value between 15 and 20 pg/ml as the predictor with the highest accuracy for developing hypocalcemia (sensitivity of 94% and specificity of 90.8%). Additionally, a decrease of between 75 and 90% of PTH concerning the initial value identified patients with postoperative hypocalcemia with a sensitivity and specificity of 93 and 90%, respectively. However, the studies included in this systematic review were heterogeneous with the time of taking postoperative PTH levels, making it difficult to establish a conclusive conclusion and develop guidelines or specific recommendations. In addition, about 70% of patients developed hypocalcemia despite normal PTH levels.⁵⁷ In 2016, Inversini and associates published a work performed on 206 postoperative total thyroidectomy patients. In this work, PTH levels correlated positively and significantly with calcium levels at 48 hours after surgery, i.e., patients had higher serum calcium levels at higher PTH levels. These authors concluded that patients with PTH levels equal to or higher than ten pg/ml (three to six hours after surgery) allow patients to be discharged early and safely due to the low risk of developing postoperative hypocalcemia.⁵⁸ On the other hand, intraoperative PTH measurements (10 minutes after thyroid resection) allow for predicting the risk of postoperative hypocalcemia without an additional advantage over postoperative measurements between the first and fourth hour after surgery.⁵⁹

Most studies show that PTH levels below double digits (< 10 pg/ml) within the first six postoperative hours are statistically significant predictors of postoperative hypocalcemia.

Finally, calcium supplementation with or without vitamin D is an appropriate and cost-effective strategy to decrease the risk of postoperative hypocalcemia and hospitalization time after thyroidectomy, with the risk of overtreatment of patients who will not develop hypocalcemia.^{60,61} Therefore, the use of this evidence-based strategy in patients at high risk of postoperative hypocalcemia (such as patients with Graves' disease, central compartment dissection in thyroid cancer, reoperations, etc.) could be helpful for such purposes.

Recommendation 11. *It is recommended that serum magnesium levels be measured and replaced, if necessary, in the immediate postoperative period in patients undergoing thyroid surgery (low level of evidence; weak grade of recommendation).*

Magnesium is an electrolyte that regulates serum calcium concentrations due to its promoting effect on the synthesis and release of parathyroid hormone (PTH) and the modulation of renal calcium excretion. Thus, the state of hypomagnesemia reduces PTH secretion, perpetuating the state of hypocalcemia.^{62,63} The incidence of hypomagnesemia in the preoperative and immediate postoperative period after total thyroidectomy is reported to range from 24% to 23-70%, respectively.^{64,65} Some studies have identified hypomagnesemia as a preoperative risk factor for the development of prolonged transient hypocalcemia in postoperative total thyroidectomy patients, in contrast to other reports in which this risk factor has not been identified.⁶⁶⁻⁶⁹ In the most recent meta-analysis by Chen et al., hypomagnesemia was identified as a risk factor for postoperative prolonged hypocalcemia with an odds ratio (OR) of 2.9 (95% CI 1.9-4.2; $p < 0.00001$).⁷⁰ Although the evidence regarding preoperative magnesium supplementation is sparse, the benefit is cost-effective and appears to outweigh the risks.

What is the appropriate time to initiate hormone replacement with levothyroxine postoperatively in patients undergoing thyroidectomy or with pre-existing hypothyroidism?

Recommendation 12. *It is recommended that levothyroxine be started immediately postoperatively in patients with total thyroidectomy or pre-existing hypothyroidism. Thyroid-stimulating hormone (TSH) levels should be monitored in the following 4-6 weeks to adjust this substitution scheme (high evidence level; strong recommendation grade).*

Regardless of the scheme used for the calculation of the substitution dose (based on weight, age, gender, or body mass index),⁷¹ recommends starting levothyroxine at the

total dose or progressively (increments of 12.5 to 25 micrograms/day) in cases of advanced age, cardiovascular disease or other associated comorbidities.⁷² The most reliable parameter to guide changes in hormone replacement is TSH. This should be evaluated at four to six weeks since this is the time necessary to achieve stable T4 levels due to its prolonged half-life (seven days).⁷³

CONCLUSIONS

This document includes a series of recommendations that include the three stages of the perioperative period to provide optimal care for patients who will undergo thyroid resection, including the scientific evidence available at the time. The authors recognize that some of the recommended tools are not always available in our country; however, the objective of the present work is to inform and disseminate the best practices available regarding thyroidectomy, to improve the surgical care of patients in Mexico, and to reach as far as possible the international standards of care for this group of patients.

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