



KINGDOM OF MOROCCO  
MOHAMMED V UNIVERSITY OF RABAT  
FACULTY OF MEDECINE  
AND PHARMACY  
RABAT



Year : 2020

Thesis N°: 107

# INCIDENCE AND PREDICTIVE FACTORS OF POST THYROIDECTOMY HYPOCALCEMIA

## THESIS

*Publicly submitted and defended on the : / /2020*

**BY**

**Mrs. Eden Ayele HABTE**

*Born on November 09th, 1994 in Addis Ababa (Ethiopia)*

*FOR THE DEGREE*

**Doctor of Medicine**

**Key Words** : Thyroidectomy; Hypocalcemia; Post-thyroidectomy complications;  
Dysphonia

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Médecine Interne - Clinique Royale  
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#### Janvier, Février et Décembre 1987

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Médecine Interne

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Pr. ADNAOUI Mohamed  
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Chirurgie Générale  
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Chirurgie Générale  
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Radiologie  
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 Rhumatologie  
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 Pédiatrie  
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### **MARS 2014**

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 CCV



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Pr. TAZI MOUKHA Zakia

Médecine Interne  
Génécologie-Obstétrique

#### **DECEMBRE 2014**

Pr. ABILKACEM Rachid\*  
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Cardiologie  
Anesthésie-Réanimation  
Chirurgie Pédiatrique  
Psychiatrie  
Médecine préventive, santé publique et Hyg.

#### **AOUT 2015**

Pr. MEZIANE Meryem  
Pr. TAHIRI Latifa

Dermatologie  
Rhumatologie

#### **PROFESSEURS AGREGES:**

##### **JANVIER 2016**

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Ophtalmologie  
O.R.L  
O.R.L

##### **JUIN 2017**

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Anatomie  
O.R.L  
Médecine préventive, santé publique et Hyg.  
Immunologie

##### **NOVEMBRE 2018**

Pr. AMELLAL Mina  
Pr. SOULY Karim  
Pr. TAHRI Rjae  
\*Enseignants Militaires

Anatomie  
Microbiologie  
Histologie-Embryologie-Cytogénétique



## 2 - ENSEIGNANTS-CHERCHEURS SCIENTIFIQUES

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Mise à jour le 04/02/2020

Khaled Abdellah

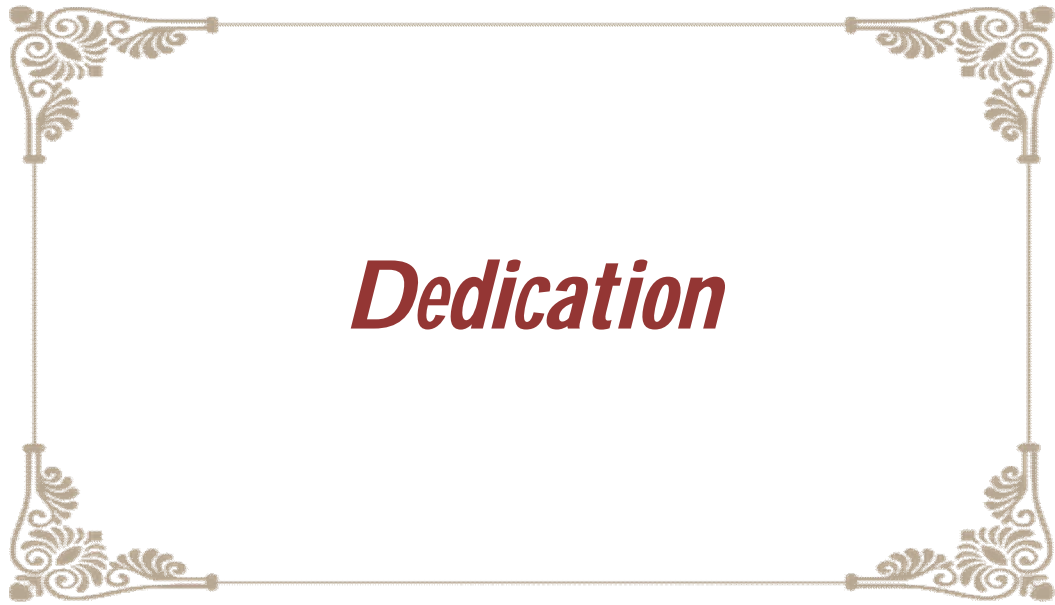
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Abdellah KHALED



***To my beloved parents***

*This study is wholeheartedly dedicated to my wonderful parents, who have been my source of inspiration and gave me strength when I thought of giving up. Thank you for loving me and providing me with your moral, spiritual support.*

*I love you papa and maman.*

***To my amazing sisters***

*I am forever grateful for you girls more than I can express with words. Thank you for being my inspiration, my soul mates, and believing in me even when I didn't believe in myself.*

*I love you very much.*



### ***To my friends***

*To those who have encouraged me, supported me and shared the ups and downs of this journey called life with me. I am lucky to have crossed paths with you and I appreciate you. And a special thank you to Anna Isabelle for your advice, support and love. Because you always understood, thank you.*

### ***To God***

*And last but not least, I would like to dedicate this thesis to the almighty God. Thank you for the guidance, strength and giving me a healthy life. None of this would have been possible without him, I give praise and thanks.*



# *Acknowledgements*





***To the president of the jury***

***Pr. IFRINE Lahssan***

***Professor of General and Endocrine surgery***

*You do us a great honor by agreeing to judge our thesis.*

*With great admiration your competence, rigor and human qualities.*

*You serve as an example for us of righteousness and seriousness*

*in the exercise of the profession of medicine .Kindly accept*

*professor, our deep appreciation, respect and thanks.*



***To our thesis supervisor  
Professor EL. MALKI Hadj Omar  
Professor of General and Endocrine surgery***

*For your sound advice, unwavering support and competence  
at every step of this study. We appreciate your unparalleled  
kindness and thank you for your tireless effort you put into this work.  
Kindly accept the expression of our deepest gratitude,  
respect and our sincerest thanks.*



***To our member of jury***

***Pr. IRAQI Hind***

***Professor in Endocrinology and Metabolic diseases***

*Thank you for the great kindness with which you welcomed me as well as for having accepted to judge this work. We express our outmost respect and admiration for your professional skills, your praised human qualities and generosity. For this honor, accept my greatest gratitude.*



*To our member of jury*

***Pr. CHARIF CHEFCHAOUNI Al Montacer***

***Professor of General and Endocrine surgery***

*It is an honor and a great privilege to have  
you in our thesis jury. Rest assured, dear professor  
of my deep recognition and my highest esteem.*



# ***Abbreviations***

## ABBREVIATIONS

<b>CT</b>	: Completion Thyroidectomy
<b>EOP</b>	: Endocrine Ophthalmopathy
<b>FNAB</b>	: Fine Needle Aspiration Biopsie
<b>IJV</b>	: Internal Jugular Vein
<b>iPTH</b>	: Intact Parathyroid hormone
<b>LND</b>	: Lymph Node Dissection
<b>MB:</b>	Maladie de Basdow
<b>MND</b>	: Modified Selective Neck Dissection
<b>MNG</b>	: Multinodular Goiter
<b>PTGs</b>	: Parathyroid Glands
<b>RND</b>	: Radical Neck Dissection
<b>SCM</b>	: Sternocleidomastoid Muscle
<b>SN</b>	: Solitary Nodule
<b>SND</b>	: Selective Neck Dissection
<b>TRAb</b>	: TSH-Receptor Auto-Antibodies
<b>TSH</b>	: Thyroid Stimulating Hormone
<b>TT</b>	: Total Thyroidectomy
<b>US</b>	: Ultrasound



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# ***Introduction***

Thyroidectomy is considered to be a common operative procedure in endocrine surgery. The most prevalent complications of thyroid surgery include hypocalcaemia and damage to the recurrent nerves. Hypocalcaemia occurs transiently in 20 to 30% of the time or in rare cases permanently in 1 to 4 % of the time. While damage to the recurrent laryngeal nerve resulting in dysphonia occurs transiently in 5 to 11% of operations or permanently in 1 to 3.5% of operation [1].

In addition post-operative hematoma and acute dyspnea are exceptional but life threatening complications in thyroid surgery. These complications cause a prolonged hospitalization but also increased cost of treatment [2], and for patients who eventually develop permanent hypocalcaemia, a life time supplement of calcium.

Post thyroidectomy hypocalcaemia is due essentially to hypoparathyroidism which is the result of direct injury, obstruction of venous drainage, devascularization, or inadvertent excision of the parathyroid gland [3]. However normal postoperative response to stress including hemodilution and antidiuretic secretion also lowers total serum calcium levels [4;5]. Post operative calcemia can either be asymptomatic specially if the calcium level is mildly reduced or can be symptomatic going from minor hypocalcemic signs such as Trousseau's and Chvostek's Signs, muscle spasm and parasthesia to major complication resulting in hypocalcemic tetany. Hypocalcemic tetany is characterized by extensive spasm of skeletal muscle, involving especially the muscles of the extremity and larynx. In tetany, laryngospasm becomes so severe that the airway is obstructed and fatal asphyxia is produced [6].

The traditional method for detecting post-operative hypocalcaemia include frequent monitoring of serum calcium or ionized calcium and the detection of hypocalcemic symptoms [7]. Postoperative phosphate could also be assessed as a biochemical factor as it varies in parallel to post-operative calcemia [8]. Nonetheless Intraoperative or early post-operative intact parathyroid hormone (iPTH) are reliable for predicting postoperative hypocalcaemia [9;10], however due to the cost and lack of availability the use iPTH is limited. Many endocrine surgeons are interested in predicting hypocalcaemia early to prevent serious complications and eventually begin treatment to hasten hospital discharge.

The aim of this retrospective observational study was to determine the incidence of hypocalcaemia in patients undergoing different type of thyroidectomy for different pathologies, in order to determine which are the factors that could be used as predictive indicators of post-operative, transient or permanent hypocalcaemia. Thus helping us to prevent and manage them better.



# ***Materials and Methods***

## **I-PATIENTS:**

From January 2007 to December 2018, 461 patients underwent thyroid surgery at the surgical Department A in Ibn Sina Hospital for different thyroid pathologies. Patients with concomitant parathyroid pathology and renal failure are not included in our series. A retrospective study was conducted from the medical dossiers of the patients and computerized data when available. A data collection form that we specifically designed for our study was used (annex 1).

Patients were admitted to the department through referrals or transfers from the endocrinology department or during consultations. Upon admission, they underwent;

### **➤ Full medical interrogation;**

The patients were inquired about their age, gender, profession, type of medical Insurance, marital status, personal and family health background and evolution of current pathology.

### **➤ Physical examination;**

We proceeded with examination of the cervical region, the state of vocal cords (endoscopy or indirect laryngoscopy was performed for patients who had undergone cervical surgery or were presenting with dysphonia) and looked for the presence or absence of exophthalmoses. It will be completed with a full physical examination.

### ➤ **Biological tests:**

All patients systematically get a blood cell count, serum electrolyte levels and thyroid function test (TSH). Patients with TSH level below 0.5 mUI/L are considered to be hyperthyroid, and will go through preoperative preparation to reach euthyroidism before surgery.

Preoperative calcemia and phosphorus levels were also systematic and we considered a preoperative hypocalcaemia a serum calcium level below 85mg/l.

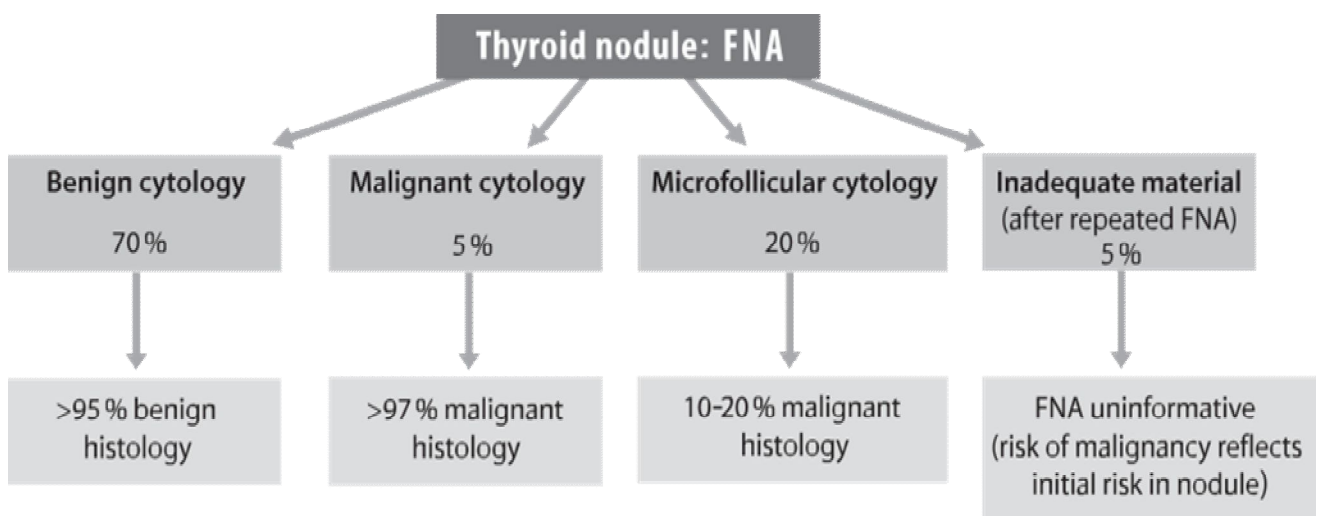
In addition, we measured calcitonin levels (suspicion of medullary thyroid cancer) and performed thyroid antibody tests (suspicion of Graves' disease) according to the case.

### ➤ **Medical imaging tests:**

- **Chest X-ray:** Is systematic for all patients, we will look for direct and indirect signs of plunging goiter such as deviation of the trachea. It can also show pulmonary metastases if present.
- **Cervical ultrasound (US):** All patients get systematically a cervical ultrasound. A thyroid gland is considered to be a large volume goiter on US if one of the measurements is >10cm. US allows to assert the nodule's existence, to measure it and to assess the context (goiter, auto-immune disease). US also allows quantitative risk stratification of malignancy using the TIRADS classification and later on EU-TIRADS score (since 2009), which goes from 1 to 5 and defines the indications for fine-needle aspiration [11].

- **Scintigraphy:** It should be reserved to low TSH patients. If the scintigraphy pattern shows the presence of diffuse thyroid overactivity with a homogeneous distribution of the tracer and reduced uptake in major salivary glands it is read as diagnostic for Graves' hyperthyroidism. If the pattern shows a normal gland uptake, a decreased uptake, a unifocal or multifocal overactive areas with reduced or suppressed uptake in the remaining thyroid tissue it is consistent with autonomously functioning thyroid nodule(s) corresponding to non-Graves' hyperthyroidism cases.
- **Cervical or Mediastinum CT scan:** these imaging tests were indicated when patients present a plunging goiter with compression signs clinically or on thoracic radiology, to determine specifically the characteristics of the goiter. And if thyroid cancer has been diagnosed (EU-TIRADS 4 or 5 on US and malignancy on FNA) patients got a CT scan, it is used for staging and assessment of the extent of the malignant thyroid tissue. CT scan can be performed systematically in addition to the US for patients with a clinical suspicion of advanced disease.

➤ **Fine needle aspiration biopsy (FNAB)** was performed for patients with suspicious thyroid nodules. Thus all nodules above 20 mm (except non compressive EU-TIRADS 2 cysts), EU-TIRADS 4 nodules above 15mm and EU-TIRADS 5 nodules above 10 mm [12] will undergo FNA. According to Bethesda system [13] the cytology reports at our institution were classified as benign follicular nodule, malignancy, suspicious for malignancy, atypia of undetermined significance or follicular lesion of undetermined significance, follicular neoplasm or suspicious for a follicular neoplasm, non diagnostic or unsatisfactory. Furthermore cytologically indeterminate nodules are now subdivided into three categories; those with the highest indeterminate risk (suspicious for papillary carcinoma), intermediate (suspicious for a follicular neoplasm) or low indeterminate risk (atypia/follicular lesion of undetermined significance) [14].



**Fig. 1:** Correlation between FNA cytology and histological diagnosis. [15;16].

## II-DIAGNOSIS:

After assessment of the physical examination, biological and imaging test our patients were given a diagnosis.

### A- Multinodular goiter:

The diagnosis of multinodular goiter (MNG) was retained in the presence of 2 or more clinically palpable nodules and/or the presence of at least 2 nodules on cervical ultrasound.

If TSH level is bellow 0.5mUI/L it will indicate on the functional status of the nodules as hyper functioning, thus indicating it's a toxic multinodular goiter [17].

### B- Solitary Nodule:

The diagnosis of solitary nodule (SN) was retained in there is only one nodule visible on cervical ultrasound. If TSH level is bellow 0.5mUI/L it will indicate that the nodules is hyper functioning resulting in toxic nodule. Patients with suspicious sonographic features (EU-TIRADS 4) will undergo FNA. Findings should be reported using the diagnostic categories outlined in the Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) [12;18].

### C- Thyroid cancer:

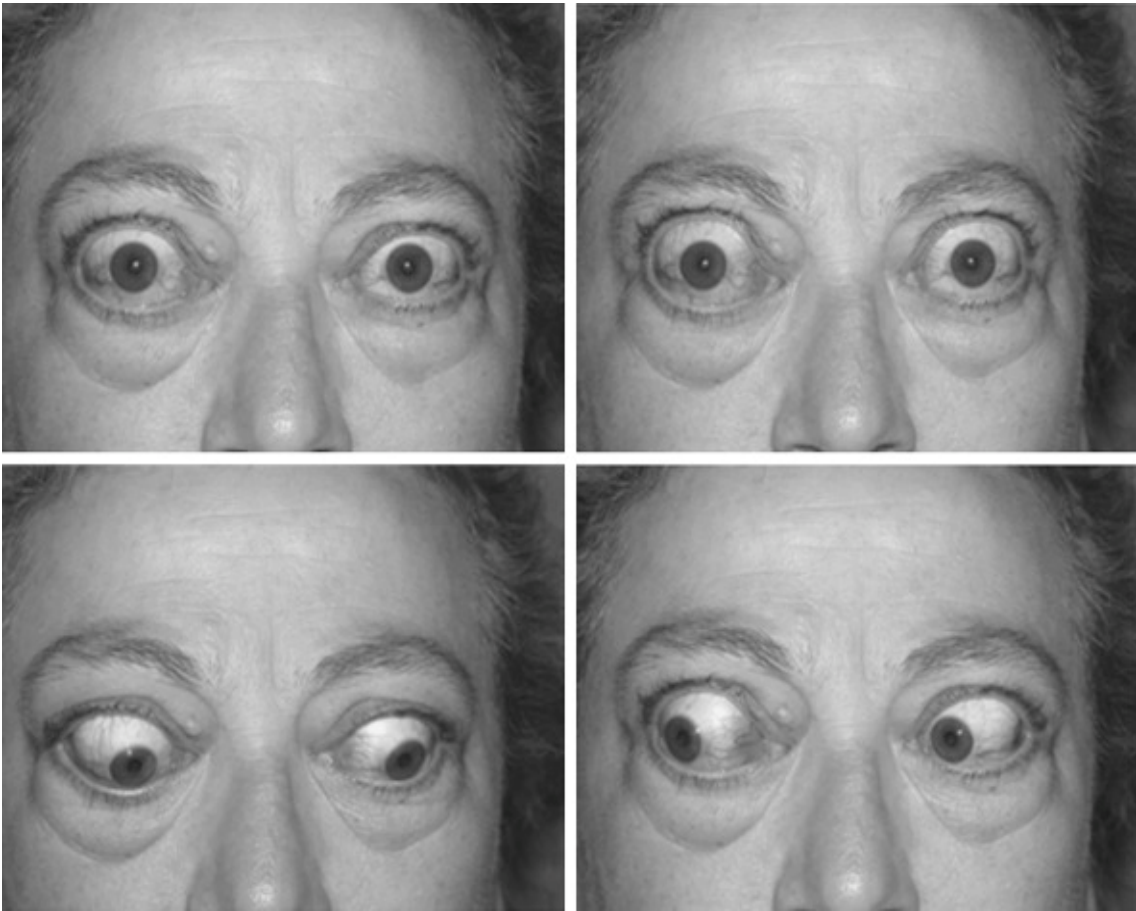
We suspect thyroid cancer in patients with risk factors for malignancy such as local or distant metastases of unknown origin, personal or family history of thyroid cancer, or irradiation before adolescence.

In addition clinically the presence of pain, dysphonia or hoarseness of the voice, rapid evolution of the pathology, nodule diameter > 4cm, firm nodules during palpation with inflammatory aspect, fixation to adjacent neck structures and presence of enlarged nearby lymph nodes suggest malignancy [19; 20].

On ultrasound we will look for characteristics of malignancy, such as ill-defined margin, irregular shape, hypoechogenicity, heterogeneity, absence of cystic lesion and/or the halo sign, the presence of calcification and invasion to adjacent organs [21 - 23]. After US evaluation of the thyroid gland, US-guided FNAB was performed and malignant cytology will confirm the diagnostics.

#### **D- Graves disease:**

Clinically we have the presence of hyperthyroidism signs: tachycardia, arrhythmia, palpitations, nervousness, anxiety and irritability, tremor, sweating, changes in menstrual patterns, increased sensitivity to heat, fatigue, muscle weakness, diffusely homogenous and vascular enlarged thyroid gland (goiter). Other symptoms may include pretibial myxoedema (thickening of the skin on the shins), and a condition caused by Graves opthalmopathy; exopthalmos, it is bilateral, axial and symmetrical [24]. A clinical score may be used to quantify the clinical symptomatology and for follow-up examination [25].



**Fig. 2** : Endocrine ophthalmopathy (EOP) in a patient with Graves' disease. Proptosis, inflammatory signs (conjunctival injection, and palpebral edema and redness, lacrimal gland edema) and eyelid retraction are quite evident [26].

On scintigraphy thyroid scans were read as diagnostic for Graves' hyperthyroidism in the presence of diffuse thyroid overactivity with a homogeneous distribution of the tracer and reduced uptake in major salivary glands

Blood tests show a raised T3 and T4 levels , low TSH, and the presence of TSH-receptor auto-antibodies [TRAb] , the dosage of TSH receptor antibodies is not systematic [27].

### **III- SURGICAL INTERVENTIONS :**

#### **A- Patients preparation :**

When the patient presents hyperthyroidism with low TSH levels ( $<0.5\text{mUI/l}$ ) he will require a preoperative preparation related to their thyroid gland, to make sure the patient is euthyroid before the surgical intervention, on average the time preparation time is 6 weeks, thus the protocol for the patients at our department is based on the administration of:

- Carbimazole (Dimazole®, Neomercazole® ) 3cp 3 times a day = 45-60 mg/day
- Propranolol (Avlocardyl®)  $\frac{1}{4}$  a  $\frac{1}{2}$  cp 3 times a day = 30 to 60mg/day

Clinical and biological monitoring is instituted until the TSH level is within normal range.

Additionally, all patients undergoing thyroidectomy will have their vocal cord function evaluated and documented prior to surgery if they present signs of compression, dysphonia and/or if it is an iterative surgical intervention [28].

Regardless of the pre-operative thyroid status all patients will have pre anesthetic evaluation.

#### **B- Surgical techniques:**

The technique we will describe refers to a capsular dissection with vessel suture ligation of a thyroid lobe, which initiates as a hemithyroidectomy but can be extended to a total thyroidectomy if indicated.

➤ **Anesthesia:**

Thyroidectomies are performed under general anesthesia with endotracheal intubation [29].

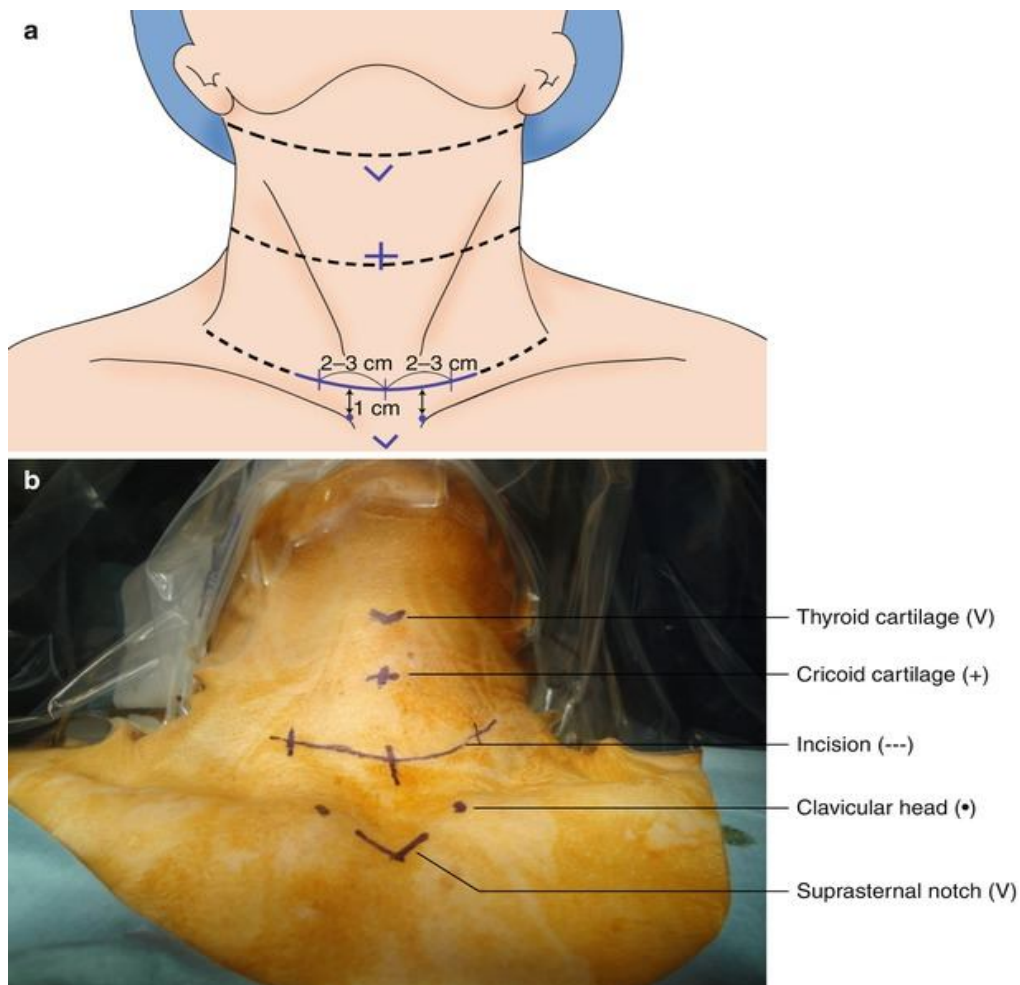
➤ **Positioning:**

The patient is placed in a supine position with the apex of the patient's head at the top of the operating bed. To help extend the neck a shoulder roll or gel pad should be placed at the level of the acromion process of the scapula. Hyperextension of the neck should be avoided, and the head should be supported to provide maximal exposure of the surgical field without hyperextension. Apart from residual local neck pain, severe frontal or occipital headache, which may persist for several weeks postoperatively before resolution, may be consistent with hyperextension, irrespective of age [28]. The patient's arms are gently tucked by either side. The bed is sufficiently moved away from their machines to provide a maximal work area.

➤ **Marking:**

After superficial palpation of the cervical region the following anatomic location will be marked with a marking pen: the thyroid notch, the cricoid cartilage, the superior edge of clavicles and the sternal notch.

A curvilinear collar-type incision is placed transversally along the Langer's line of the skin (length of between 6 cm and 8 cm) will be done approximately 2 cm or 2 finger-breadths above the superior edge of the clavicle and sternal notch. A 4 to 5 cm incision allows safe thyroidectomy in most cases and results in excellent cosmesis. However, patients with larger tumors or goiters or those with short necks will require a larger incision for optimal exposure.



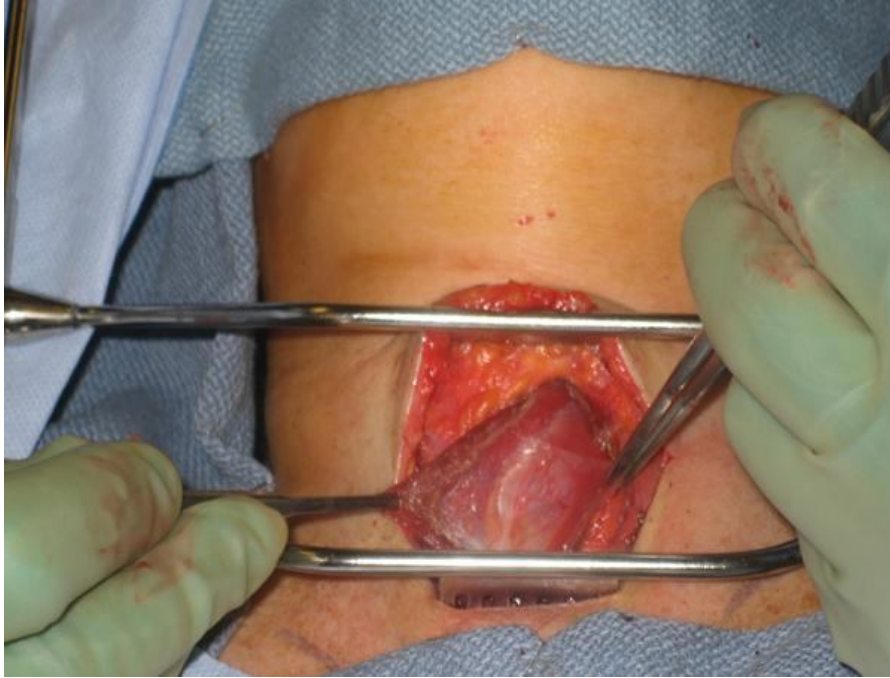
**Fig.3:** marking of the cervical region for incision [30].

➤ **Incision and exposure of the thyroid gland:**

The 1st incision which is a standard Kocher's incision is made over the marked line as described in the marking sections. A #15 blade is used to incise through the epidermis and dermis. Using a Shaw scalpel (or monopolar cautery), dissection is carried through the subcutaneous fat to the platysma. Once the level of the platysma has been identified along the length of the incision, the platysma is incised. Using the double-pronged skin hooks and the Shaw scalpel (or monopolar cautery), subplatysmal flaps are elevated superiorly and inferiorly. After elevating the subplatysmal flaps, the thyroid retractor we will be inserted cautiously without lacerating or damaging the skin edges with the retractor.

Once the strap muscles (sternohyoid and sternothyroid) and in the midline between the strap muscles the cervical linea alba is identified, using a Harmonic scalpel or monopolar cautery we will bluntly dissect through this fascia superiorly and inferiorly along the length of the sternohyoid muscle. In cases of large goiter or neoplasm, the strap muscles may be divided to aid exposure. Division of the strap muscles should be performed high (cephalad), because the innervation of the strap muscles occurs more inferiorly.

Just deep to this dissection we find the thyroid gland, and the overlying fascia should be easily identified.

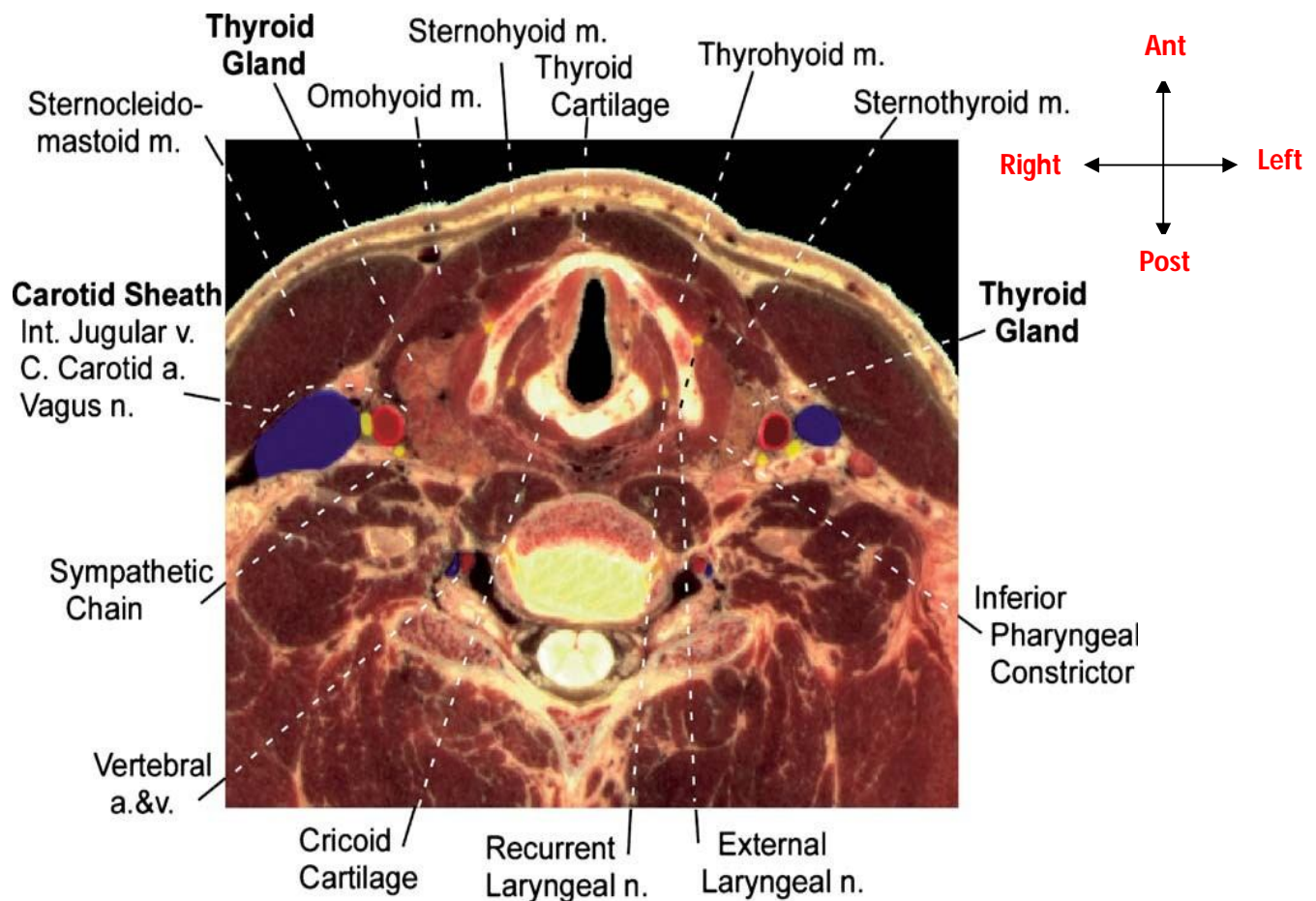


**Fig.4:** Cervical Lenea Alba [31].

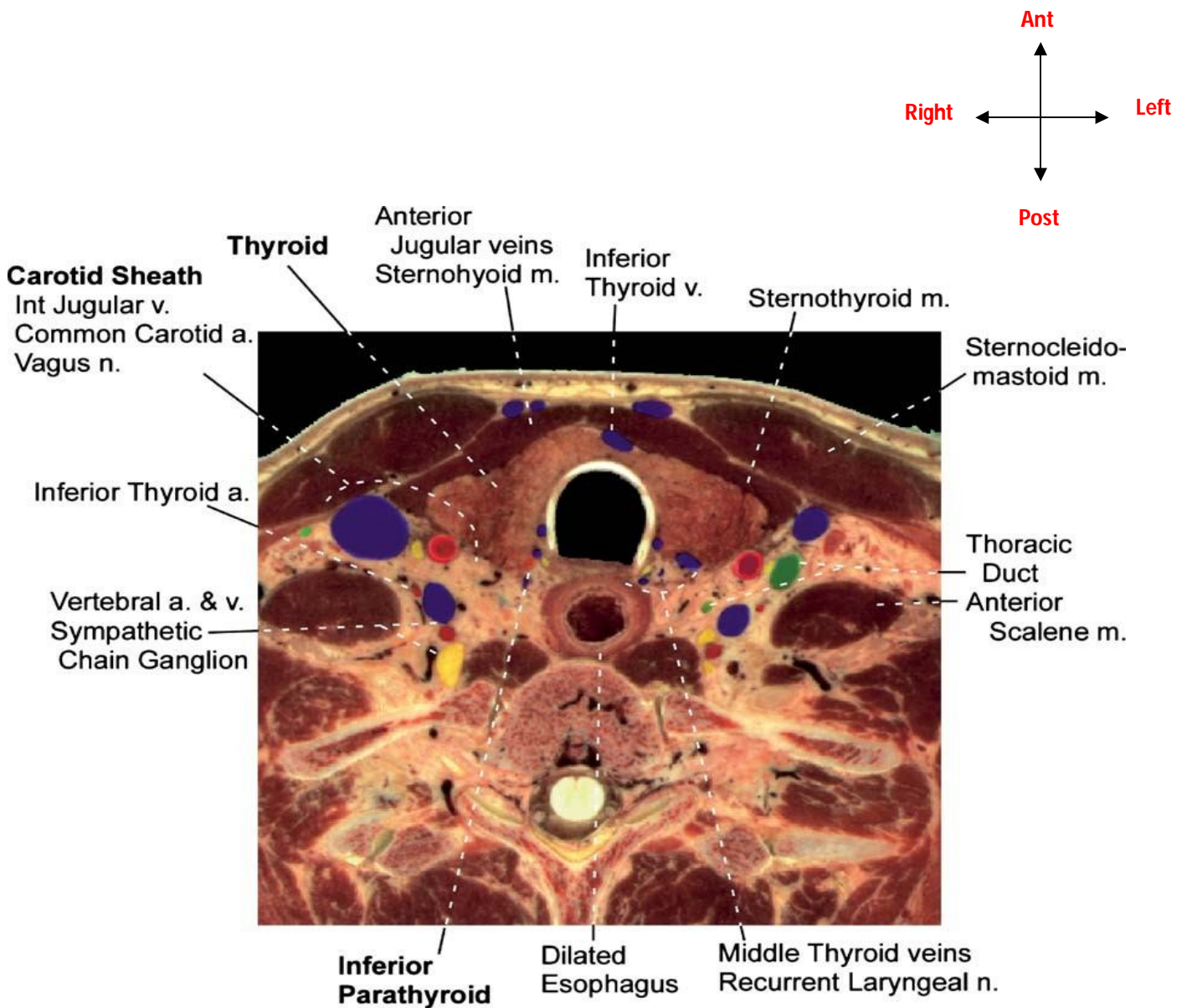
The fully developed thyroid gland extends from the level of the fifth cervical vertebra to the first thoracic vertebra and is composed of 2 lateral lobes and a central isthmus with or without a pyramidal lobe (40-50%). It weighs about 30g, being somewhat heavier in females than in males [32]. The thyroid lies in the middle layer of the deep cervical fascia and is attached from its superior-medial aspect to the thyroid and cricoids cartilages via the anterior suspensory ligament. Berry's ligament (ligament de Gruber), the posterior suspensory ligament connects the posterior-medial aspect to the first and second tracheal ring and the cricoid cartilage. The sternohyoid and sternothyroid muscles cover the thyroid gland anteriorly. Laterally the gland is related to the carotid sheath, which contains the common carotid artery, the internal jugular vein, and the vagus nerve. Posteriorly, the superior parts of the lobes of the thyroid are related to the longus colli (muscle long du cou) and longus capitis

muscles (muscle long de la tete). Medially, the superior part of the thyroid is related to the larynx and laryngopharynx, which includes the cricothyroid and inferior pharyngeal constrictor muscles and the thyroid and cricoid cartilages. Medially, the inferior part of the thyroid is related to the trachea and the esophagus.

The tubercle of Zuckerkandl (tubercule de Zuckerlandl) extends off of the posterior and lateral aspect of the thyroid lobes [33;34].



**Fig.5:** The Thyroid gland and its relations at the level of the thyroid cartilage; Color enhancement demonstrates major arteries (red), veins (blue), and nerves (yellow). Note the close relationship of the superior pole of the thyroid gland with the carotid sheath and sympathetic chain [35].

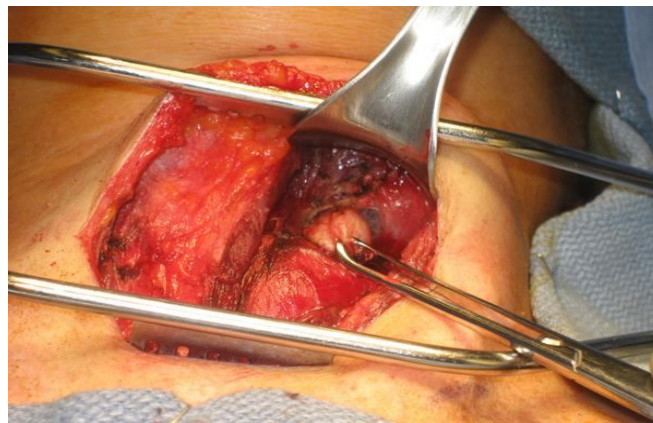


**Fig. 6:** Thyroid gland and its relations at the level of the third tracheal ring. Note the posteromedial relationships of the thyroid gland with the recurrent laryngeal nerve and middle thyroid veins. The thoracic duct (green) is atypically dilated close to where it joins the left internal jugular and subclavian veins. The inferior thyroid artery follows a looping course. In this image it is seen superior to its origin from the thyrocervical trunk of the subclavian artery. It will loop superiorly and medially before descending to join the thyroid gland near the recurrent laryngeal nerve. An inferior right parathyroid gland (orange) is evident near the recurrent laryngeal nerve and middle thyroid veins. Major nerves (yellow), arteries (red), and veins (blue) are indicated [34].

➤ **Releasing the superior pole:**

Once the thyroid gland is identified, attention should be turned to a single lobe. Using the Richardson retractors and blunt dissection, capsular dissection should be carried to the lateral aspect of the thyroid lobe, where it meets the carotid sheath fascia. Once the lateral border of the dissection has been performed, the carotid artery identified, blunt dissection may be carried out superiorly.

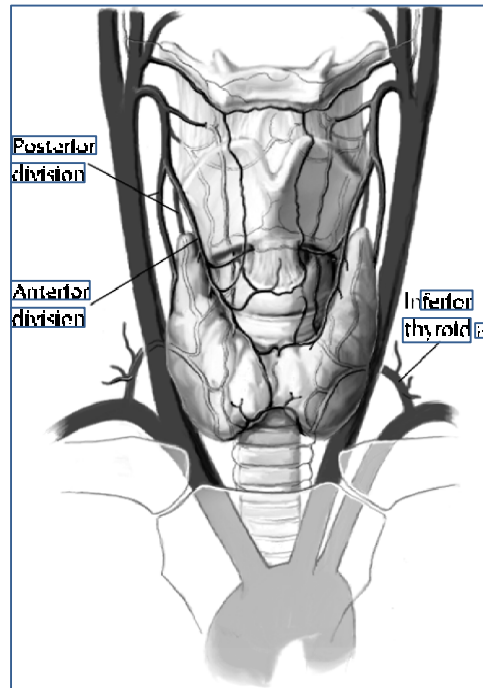
At the superior pole, care should be taken to dissect the overlying strap muscles off of the thyroid gland without injuring the subcapsular vessels. Next, the cricothyroid space should be identified and dissected. By retracting the thyroid inferiorly and medially, the strap muscles superiorly and laterally, the surgeon can allow for maximal visualization of the superior pole of the thyroid. After dissecting both laterally and medially (cricothyroid space) to the superior pole, the superior pedicle can be divided using a Harmonic scalpel, clips, or ties. Care should be taken to avoid injuring the external branch of the superior thyroid nerve [36;37].



**Fig 6:** Exposure of the superior pole [30].

In order to avoid any injury to the arteries while releasing the superior pole the surgeon should be well familiarized with blood supply of the thyroid gland. The thyroid gland has the greatest blood supply per gram of tissue, the significance is that homeostasis is a major problem of thyroid surgery [38]. The arterial supply is bilateral from both the external carotid system, through the superior thyroid artery, and the subclavian system, through the inferior thyroid branch of the thyrocervical trunk. There may be a single thyroid ima artery (artère thyroïdienne moyenne de Neubauer) that arises from the brachiocephalic artery, the thyroïde ima artery (also known as thyroid artery of Neubauer ) can provide an arterial supply through the inferior border of the isthmus in 2-12% of patients [39]. It branches from either the innominate, subclavian, right common carotid, internal mammary, or the aortic arch.

The inferior thyroid artery takes a looping course. It ascends along the anterior scalene muscle. It turns medially to pass posteriorly to the carotid sheath and usually posteriorly to the sympathetic trunk as well. It descends along the longus colli to reach the inferior pole of the thyroid. There it passes to the thyroid either anteriorly or posteriorly to the recurrent laryngeal artery. At the thyroid, the artery branches into superior and inferior branches. The superior branch ascends on the posterior part of the gland to anastomose with the posterior branch of the superior thyroid artery. The inferior branch supplies the inferior part of the gland as well as the inferior parathyroid glands. The inferior thyroid artery may be absent on either side. There is evidence that there are anthropologic differences in the incidence of thyroid ima arteries, as well as in the symmetric origin of the superior thyroid arteries [40].



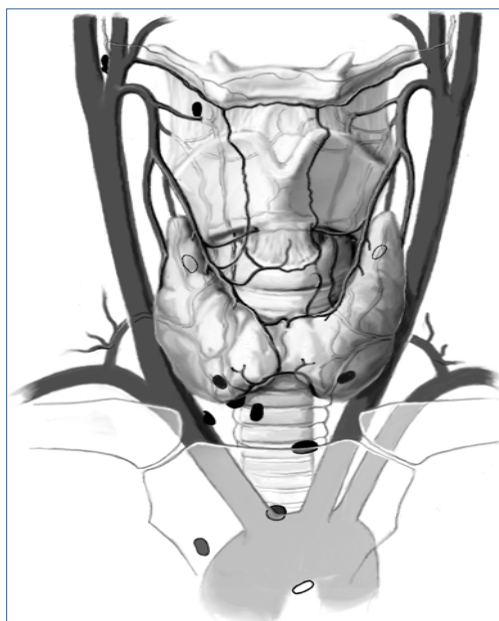
**Fig. 7 :** Arterial supply of the thyroid derived from the four main vessels of the gland. Note the anterior and posterior divisions of the superior artery. The inferior thyroid artery comes from a posterolateral position to enter the thyroid gland close to the recurrent laryngeal nerve [34].

➤ **Identifying the parathyroid glands:**

Once the dissection of the posterior part of the thyroid lobe begins, the surgeon and assistant residents should be vigilant in identifying the parathyroid glands. There are normally two pairs of parathyroid glands, located along the posterior aspect of the thyroid gland, the superior parathyroid glands normally lie at the level of the middle third of the thyroid, found cephalad to the tubercle of Zuckerkandl and can also be found adjacent to the superior pole. While the inferior parathyroid glands lies at the level of the inferior third of the thyroid, usually located in a 1 cm radius around the inferior pole of the thyroid gland and almost always anterior to the plane of the recurrent laryngeal nerve. Accessory

parathyroid glands, occur 3-7% and fewer than 4 glands are present in 3-6% of patients [41]. Aberrant or ectopic glands can also be present if the glands descend incompletely or too far. Possible locations for parathyroid glands include the anterior or posterior mediastinum, carotid bifurcation, as well as the retroesophageal, retropharyngeal, or retrolaryngeal regions [42].

Generally, the superior parathyroid glands are supplied by the inferior thyroid artery, the superior thyroid artery, or both. Anastomotic connections within the thyroid allow both vessels to contribute, especially to the superior parathyroid glands. A number of methods have been advocated for localizing the glands. These include ultrasonography [43], intraoperative methylene blue [44], and technetium sestamibi scans [45].



**Fig. 8 :** Possible localizations of ectopic parathyroid adenomas. Most of them are surgically accessible by a regular cervicotomy [34].

After identifying the glands, they should be carefully dissected from the thyroid and left in the thyroid bed. In the event of accidental avulsion of a parathyroid gland or compromising its blood supply, the affected parathyroid gland will be removed and placed within a specimen cup on ice or saline. The surgeon will then consider auto-transplantation of the gland in the sternocleidomastoid muscle [46].

On another note parathyroid incidentaloma which is an enlarged parathyroid glands discovered at the time of surgery, will be removed as it may represent an early pathological stage of a hyperfunctioning parathyroid glands, before biological findings [47;48]. Other normal parathyroid glands will be preserved [49].

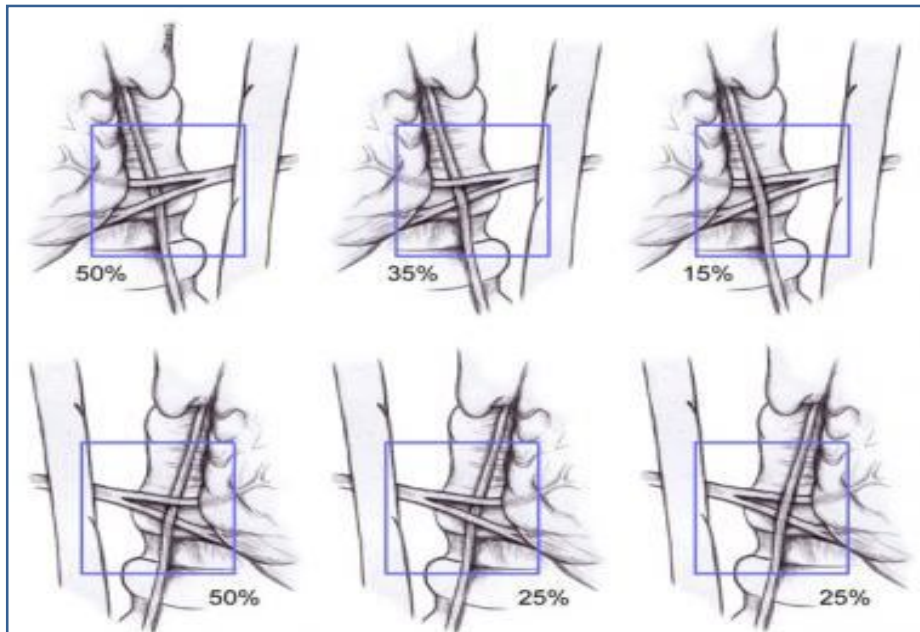
➤ **Identifying the recurrent laryngeal nerve:**

- **External Laryngeal Nerve**

The external laryngeal is a division of the superior laryngeal nerve, a branch of the vagus. This nerve supplies the cricothyroid muscle. Since this muscle is involved in movements of the vocal apparatus, damage to the nerve will impair phonation. The nerve may run near the superior pole of the thyroid on the way to its target. The external laryngeal nerve is frequently entrapped in the vascular pedicle that transmits the superior thyroid vessels. Consequently the nerve may be injured during the ligation of these vessels [50].

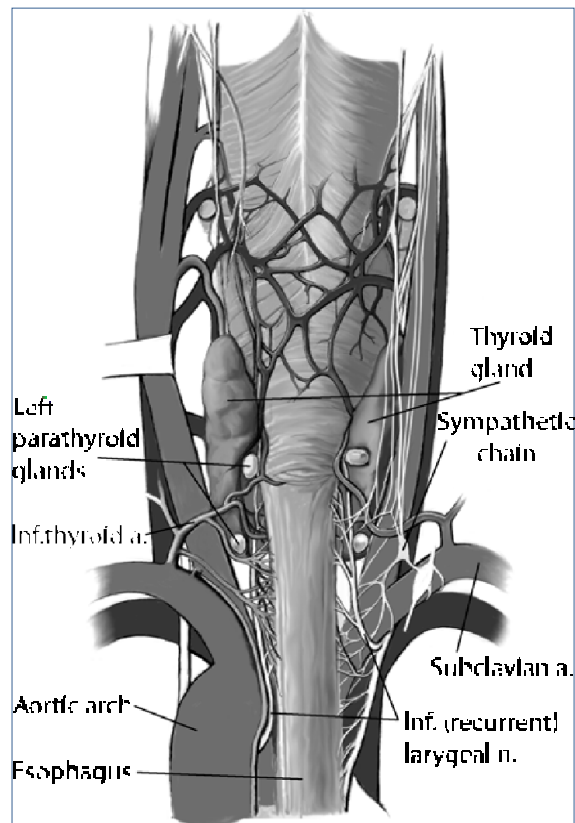
- **Recurrent Laryngeal Nerve**

The recurrent laryngeal nerve, a branch of the vagus, supplies the remainder of the laryngeal musculature as well as sensation on and inferior to the vocal folds. On the right side, the nerve loops posteriorly to the subclavian artery to ascend obliquely until it reaches the tracheoesophageal groove near the inferior extent of the thyroid. On the left side the nerve loops posteriorly to the arch of the aorta and ascends to the larynx in the tracheoesophageal groove. The nerve may divide into a number of branches that also supply the trachea and esophagus [51]. The nerve has a very close relationship with the inferior thyroid artery, where it might lie either anteriorly or posteriorly to the vessel. Because the left inferior thyroid artery may be absent in 6% of individuals, the identification of the recurrent laryngeal nerve may be more complicated [52]. The nerve may also be closely related to or within the ligament of Berry (ligament de Gruber). Care must be taken in both retraction and division of the ligament to ensure that the nerve is preserved. There are some cases where the nerve may run through the substance of the gland [53;54].



**Fig. 9:** Inferior thyroid/recurrent laryngeal nerve relationship [30].

In a small number of individuals (approximately 1%) the right subclavian artery arises distally from the arch of the aorta [55]. As a consequence the right recurrent laryngeal nerve is not pulled into the thorax by its relationship with the subclavian artery. This non-recurrent right laryngeal nerve passes directly to the larynx posterior to the common carotid artery. It runs parallel to the inferior thyroid artery and can ascend for a short distance in the tracheoesophageal groove [34]. It is, therefore, at risk for injury during surgery.



**Fig. 10 .** Schematic dorsal view shows the course of the inferior laryngeal nerve in relation to the inferior thyroid artery, the thyroid gland, and the parathyroid glands [34]

The vagus nerve and sympathetic trunk are within or closely related to the carotid sheath. The vagus nerve may receive some of its blood supply from the inferior thyroid artery [53]. Consequently, the artery should not be ligated too close to its origin. Lymph node dissection along the carotid artery and near the vertebral artery or any manipulation near the superior pole of the thyroid gland should also be performed with care to ensure that the cervical sympathetic chain ganglia are not damaged or removed.

Variations in the anatomy and location of the recurrent laryngeal nerves (RLNs) can exist. During surgery, a few anatomic landmarks can assist in identification of the nerves. The Tubercle of Zuckerkandl marks the posterolateral aspect of the thyroid lobe and is most often found lateral to the recurrent laryngeal nerve. The tubercle can be found in 80% of thyroids and when found can lead directly to the recurrent laryngeal nerve, as 93% of the nerves are found medial to this tubercle [56;57]. Most often, the nerve is found in a groove between the tubercle and the lobe of the thyroid gland [58].

The left and right nerve follow closely with the course of the inferior thyroid artery, and this landmark can also help identify the nerve. While comparing the identification of the nerve from a superior-to-inferior approach (from its insertion into the larynx) to an inferior-to-superior approach (identification at the inferior pole) a lower rate of hypoparathyroidism was found using the superior to inferior approach for identifying the RLN. However, while this was a prospective trial,

It was not randomized and could be confounded by both surgeon preference/experience and the indication for the thyroidectomy [59].

Removal of large thyroid tumors may require division of the infrahyoid muscles. Care must be taken to identify the branches of the ansa cervicalis that supply these muscles. The course of the ansa as it descends from the hypoglossal nerve is highly variable. Normally, a superior division of the muscles will ensure the preservation of the nerve supply.

Once the nerve is identified anatomically, its identity and integrity may be confirmed with nerve stimulation if the material is available. The course of the nerve should be bluntly dissected using the Reinhoff or a right angle clamp.

A sufficient portion of the nerve should be dissected to ensure its safety during dissection and removal of the thyroid gland.

➤ **Removing the thyroid gland:**

After identifying the recurrent laryngeal nerve, the thyroid gland can be removed. Berry's ligament (ligament de Gruber) defines the posterolateral attachment of the thyroid gland. Blunt dissection can be used to further expose this fascial attachment. Then a harmonic scalpel can be used to transect the ligament. Usually a minimal amount of thyroid tissue is left adjacent to the entrance of the recurrent laryngeal nerve into the larynx, to reduce the risk of injuring the nerve.

If the patient is undergoing a total thyroidectomy, attention should first be turned to the opposite thyroid lobe and recurrent laryngeal nerve. Once the entire specimen has been dissected and is only attached posteriorly to the pretracheal fascia, it can be removed. The removed specimen will be inspected and sent to the anatomopathology department [60].

➤ **Closure:**

A selective bipolar cautery is used to obtain hemostasis in the thyroid bed which is imperative, especially in the vicinity of the recurrent laryngeal nerve. A thin layer of thrombin mesh may be applied to the superior aspect of the bed. A suction drain is placed. The neck is then closed in a layered fashion with special attention to a meticulous skin closure for esthetical reasons [59].

After the surgery the extracted tissue will be sent to the anatomical pathology department to determine the malignant or benign characteristics, thus confirm the pathology diagnosis (cancer, multinodular goiter, Solitary Nodule or Graves Disease).

➤ **Overview : Type of interventions;**

According to the Diagnosis the surgeons performed either:

- **lobectomy or hemithyroidectomy** ,which consists of a surgical removal of a thyroid lobe with the isthmus. It could afterward be expanded to a total thyroidectomy by using the same surgical technique on the opposite side.
- **Total Thyroidectomy** (Subtotal thyroidectomy), which involves the surgical removal of all or part of the thyroid gland

Concerning Subtotal thyroidectomy, in which both lobes are removed except for a small amount of thyroid tissue (on one or both sides), it used to be done in our department however it is no longer done since 2004. Because a study [61] conducted in 2004 in our department comparing total thyroidectomy *versus* subtotal thyroidectomy found that; there was no difference between the two interventions when it came to post thyroidectomy complications rates.

- **Iterative completion thyroidectomy**, which involves removing the remaining thyroid tissue after a patient has had a previous partial thyroid resection (i.e. lobectomy). It may be done years later or it may be done soon after a lobectomy (within the next week after the 1st intervention).

In our study we classified the types of interventions into 2 groups; as bilateral thyroidectomy which includes total thyroidectomy and iterative completion thyroidectomy, and unilateral thyroidectomy which included hemithyroidectomy.

➤ **Other Considerations:**

- **Substernal goiter:**

The technique and approach for removing these goiters is very similar to a conventional thyroidectomy. Due to the fact that these goiters originate in the neck, they rarely have a mediastinal blood supply. Most often, removing substernal goiters does not require a sternotomy. Instead, they can be removed by digital dissection along the thyroid capsule.

- **Reoperative /revision thyroid surgery:**

For patients with previous thyroidectomy intervention we usually reopen the same incision made during the 1st operation. If significant scarring exists, one can consider using a trap door technique, in which dissection is carried from the lateral border of the thyroid medially to the central compartment.

- **Lymph nodes dissection:**

The current American Thyroid Association Guidelines for the management of differentiated thyroid cancer now call that a staging/prophylactic level 6 lymph node dissection for all patients undergoing thyroidectomy for thyroid carcinoma should be considered [62]. Thus on one hand patients with suspicious images on US (EU-TIRADS 4c and 5) with the presence of lymph nodes, and patients with FNAB Bethesda category 5 and 6 got systematically bilateral lymph node dissection. On the other hand, lymph node dissection was also done during intervention if lymph nodes were discovered during surgery.

The neck is conventionally divided into 6 levels (Level VII is in the superior mediastinum);

- Level I is bound by the body of the mandible above, the stylohyoid muscle posteriorly, and the anterior belly of the contralateral digastric muscle anteriorly. The revised classification uses the posterior margin of the submandibular gland as the boundary between Levels I and II as it is clearly identified on ultrasound, CT, or MRI. Level I is subdivided into Level Ia, (submental triangle) which is bound by the anterior bellies of the digastric muscles and the hyoid bone, and Level Ib (submandibular triangle).

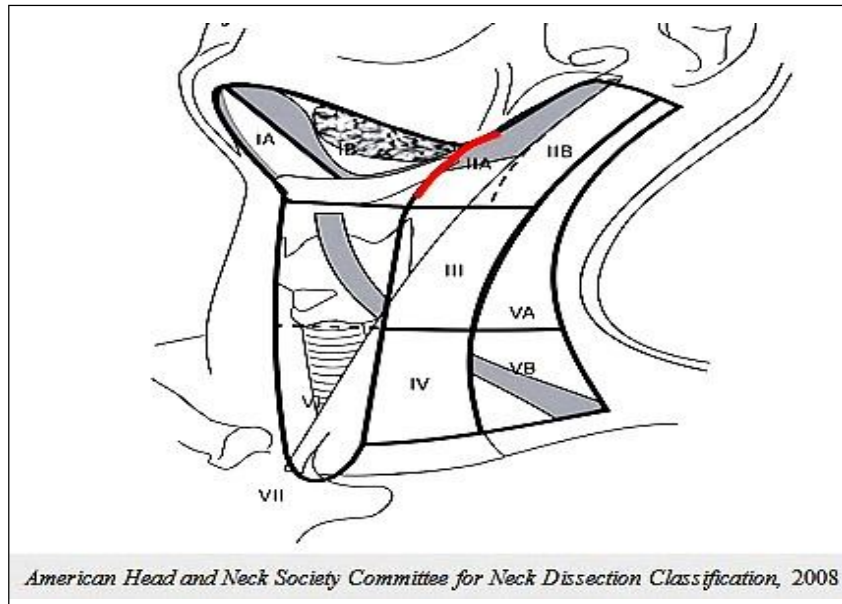
- Level II extends between the skull base and hyoid bone. The posterior border of the sternocleidomastoid defines its posterior border. The stylohyoid muscle (alternately the posterior edge of the submandibular gland) defines its anterior border. The accessory nerve (XI<sub>n</sub>) traverses Level II obliquely and subdivides it into Level IIa (anterior to XI<sub>n</sub>) and Level IIb (behind XI<sub>n</sub>).

- Level III is located between the hyoid bone and the inferior border of the cricoid cartilage. The sternohyoid muscle marks its anterior limit and the posterior border of the sternocleidomastoid its posterior border.

- Level IV is located between the inferior border of the cricoid cartilage and the clavicle. The anterior boundary is the sternohyoid muscle, and the posterior border is the posterior border of sternocleidomastoid.

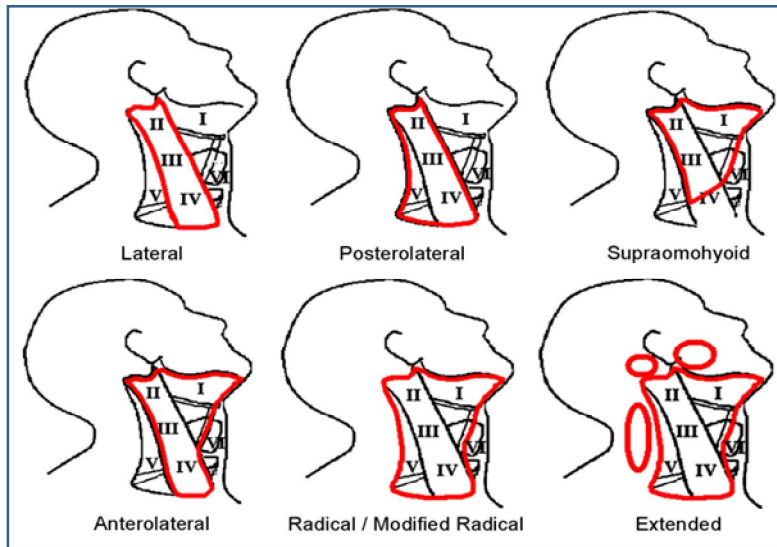
- Level V is bound anteriorly by the posterior border of the sternocleidomastoid, and posteriorly by the trapezius muscle. It extends from the mastoid tip to the clavicle and is subdivided by a horizontal line drawn from the inferior border of the cricoid cartilage into Level Va superiorly, and Level Vb inferiorly.

- Level VI is the anterior, or central, compartment of the neck. It is bound laterally by the carotid arteries, superiorly by the hyoid bone, and inferiorly by the suprasternal notch.



**Fig. 11:** Classification of cervical nodal levels [63].

Neck Dissection Classification ; Neck dissection operations are classified according to the cervical lymphatic regions that are resected. It has been proposed that neck dissections be more logically and precisely described and classified by naming the structures and the nodal levels that have been resected [64].



**Fig. 12 :** Common types of neck dissection [63].

Selective neck dissection (SND): is done for N0 necks (no clinical evidence of neck nodes) or for very limited cervical metastases. Central neck dissection encompasses only Level VI.

Comprehensive or therapeutic neck dissection: involves surgical clearance of Levels 1-V and may either be a radical (RND) or modified (MND) neck dissection. RND includes resection of sternocleidomastoid muscle (SCM) and accessory nerve (XI<sub>n</sub>) and internal jugular vein (IJV). MND preserves SCM and/or XI<sub>n</sub> and/or IJV. MND type I entails preservation of 1/3 (usually XI<sub>n</sub>), MND type II entails preservation of 2/3 (usually XI<sub>n</sub> and IJV), with MND type III all 3 structures are preserved. MND type II is most commonly done and is oncologically acceptable in the absence of adherence of cervical nodal metastases to XI<sub>n</sub> or IJV.

Extended neck dissection: includes additional lymphatic groups (parotid, occipital, Level VI, mediastinal, retropharyngeal) or non-lymphatic structures (skin, muscle, nerve, blood vessels etc.) not usually included in a comprehensive neck dissection.

## C- Thyroidectomy indications:

In general thyroidectomy is indicated as a 1st intention therapy (after euthyroidism is reached) for a young patient presenting a large volume goiter with compression signs and/or severe hyperthyroidism or as a secondary treatment after inefficiency or complication of the medical treatment (toxic effect of the anti thyroid drugs [65]) of thyroid pathologies.

Thyroidectomy is usually performed for the following reasons;

- As therapy for symptomatic thyroid masses or goiters; severe hyperthyroidism, cardiovascular complications and severe graves ophthalmopathy not responding to medical treatment [66].
- To establish a definitive diagnosis of a mass when cytologic analysis after fine-needle aspiration biopsy (FNA) is either non diagnostic, equivocal, or indeterminate.
- To treat malignant thyroid tumors (thyroid cancer) [67].
- For patients with compressive symptoms including dysphagia, dyspnea, shortness of breath, and/or hoarseness, to alleviate pressure symptoms or respiratory difficulties associated with a benign or malignant process.
- To remove large substernal goiters and sometimes for aesthetic concerns due to a goiter may also be an indication for thyroidectomy.

When it comes to the type of intervention: Total thyroidectomy is indicated for large volume multinodular goiters, Graves's disease that did not respond to medical treatment and thyroid cancer. It will be completed with a bilateral neck dissection for thyroid cancer. Isthmo-lobectomy on the other hand is indicated for benign solitary nodule. Homolateral neck dissection might be indicated if lymph nodes are present.

## IV- POST SURGICAL PROCEDURE :

### A- Clinical monitoring

Patients are monitored twice daily. Clinically we will supervise; the pulse, blood pressure, breathing, temperature, the state of the wound (detect a wound infection), presence of hematomas and the state of the drainage probe.

We will also look for post-operative hypocalcaemia signs such as: numbness, tingling of the fingers and toes, intense anxiety occurring soon after surgery. Chvostek's sign; which is the increased irritability of the facial nerve, manifested by twitching of the ipsilateral facial muscles on percussion over the branches of the facial nerve. Nevertheless Chvostek's sign is not a specific sign of hypocalcemia, some studies show that individuals with normocalcemia or hypercalcemia were significantly more likely to have a positive Chvostek sign than individuals with hypocalcaemia [68].

We will check for dysphonia as well by evaluating the patient's voice.

### B- Biological monitoring

Post operatively we analyzed serum calcium and phosphorus levels on Day 1 (24h) and Day 2 (48h). For patients whose calcium level is below 70mg/l and/or phosphorus level over 60 mg/l we systematically do a dosage of the PTH level.

We consider as post thyroidectomy hypocalcaemia patients who presented calcemia level  $< 80 \text{ mg/l}$  ( $< 2 \text{ mmol/l}$ ), on one of the 2 consecutive dosages done on day1 and day 2 postoperatively. For patients with hypocalcaemia on day 1 or day 2 we will proceed to measure serum calcium level on day 5, day 10, day 15, day 30, 3<sup>rd</sup> month, 6<sup>th</sup> month, 9<sup>th</sup> month and 12<sup>th</sup> month.

- **Hypocalcaemia treatment:**

Post-operative replacement therapy was given upon observation of clinical hypocalcaemia symptoms no matter the calcium level or if calcium levels was below 70mg/l with or without clinical symptoms, thus;

- If calcium level is between 75mg/l and 80mg/l without clinical hypocalcaemia symptoms, we do not give any replacement treatment.
- If serum calcium is < 80 mg/l with hypocalcaemia symptoms then we give calcium gluconate (Rocaltrol ®)500mg 2 to 3 times /day, if its bellow 75mg/l we add vitamin D (Unalpa® )0.25 ug/j. If its bellow 70 mg/l or for patients with severe hypocalcaemia symptoms, we increase the Unalpa up to 1 ug/j.

For patients who presented hypocalcemic tetany it requires intravenous calcium than eventually the treatment is oral.

- **Thyroid hormones:**

Hormonal replacement therapy for thyroid hormones will also be started, thus we start systematically with Levothyroxine 125ug/day.

- **Dysphonia treatment:**

Patients who presented post-operative dysphonia were given steroids; prednisone 60mg/j. Speech therapy will proceed as soon as possible. In addition laryngoscopy will be performed when the state of the patients allows it.

- **Hematomas and hemorrhages:**

Patients who present post-operative hematomas or hemorrhages will undergo emergency reintervention to relieve pressure. If it's an absolute emergency, it could be done at the bed of the patient until we get the patient to the operating room.

## V-FOLLOW UP :

The follow up of patients that underwent surgical thyroid intervention is done regularly through consultations, (which are done on a specific day of the week). All patients were monitored minimum up to 12 months after their surgery, thus these consultations allow us to;

-Do a follow up on a postoperative hypocalcaemia with repeated control of serum calcium level to determine if it is a transient or permanent hypocalcaemia. We consider as transient hypocalcaemia, patients who presented calcemia level < 80 mg/l on 2 consecutive dosages at J1 and J2 postoperatively but eventually normalized their calcium levels before 12 months without the need of replacement therapy for at least 1 month. We considered permanent hypocalcaemia; the need to maintain calcium supplementation for more than 12 months after surgery and readjust the dosage of the replacement treatment according to the severity of the symptoms and calcemic level.

- Do a follow up on a post-operative dysphonia and determine as well if its transient or permanent, we considered it to be permanent if the dysphonia persisted after 12 months post-surgery. We can also assess the progression of the speech therapy and for some patient, consider the possibility of a surgical intervention to treat the dysphonia.

- Readjust the replacement treatment (Levothyrox®) that were instituted to replace the thyroid function based on the TSHus level .We do a clinical and biological check up every 6 to 8 weeks and dosage is adjusted accordingly to the TSH level by increasing or decreasing by 25ug/j .

## VI- STATISTICS:

To conduct this study we used Excel and SPSS version 13.0 2006. Qualitative variables are represented by frequencies and percentages. Quantitative variables are represented in means +/- standard deviation (SD) or medians with interquartile ranges (IQR), the Kolmogorov-Smirnov test was used to assess the normality of the data distribution. Means were compared using the independent T test when the quantitative variables were independent and the paired sampled T test when they were dependent of a factor. Differences in frequencies between groups and statistical significance of the different factors were calculated using Fisher's exact test or CHI 2. Variables with  $p$  value  $< 0.2$  were selected for use in the multivariate analyses. Multivariate analysis was performed by a multivariate binary logistic regression model by means of a forward stepwise method. Odds ratio and 95% CI for each variable and a  $p$  value  $< 0.05$  was considered statistically significant.

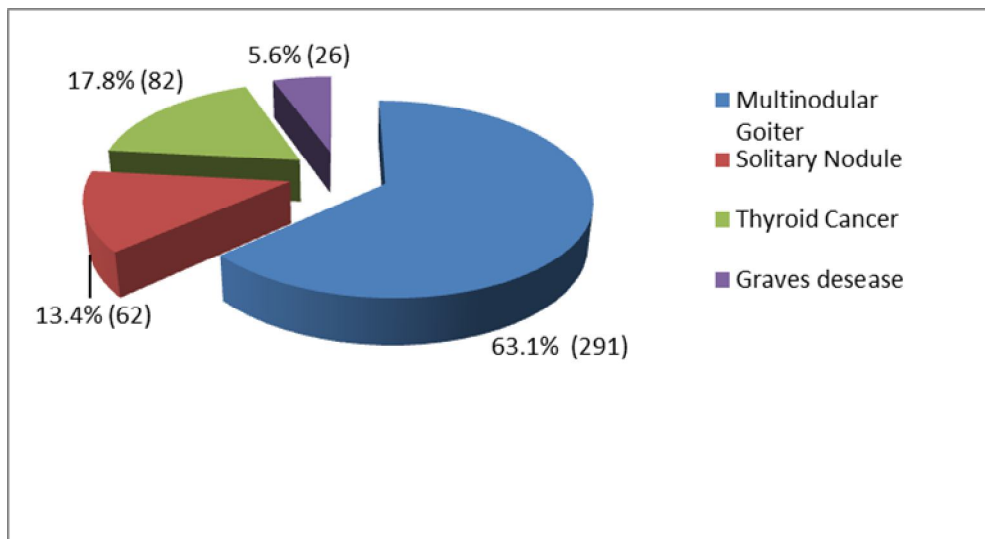


***Results***

## I- DESCRIPTIVE STATISTICAL ANALYSIS:

### A- Patients demography:

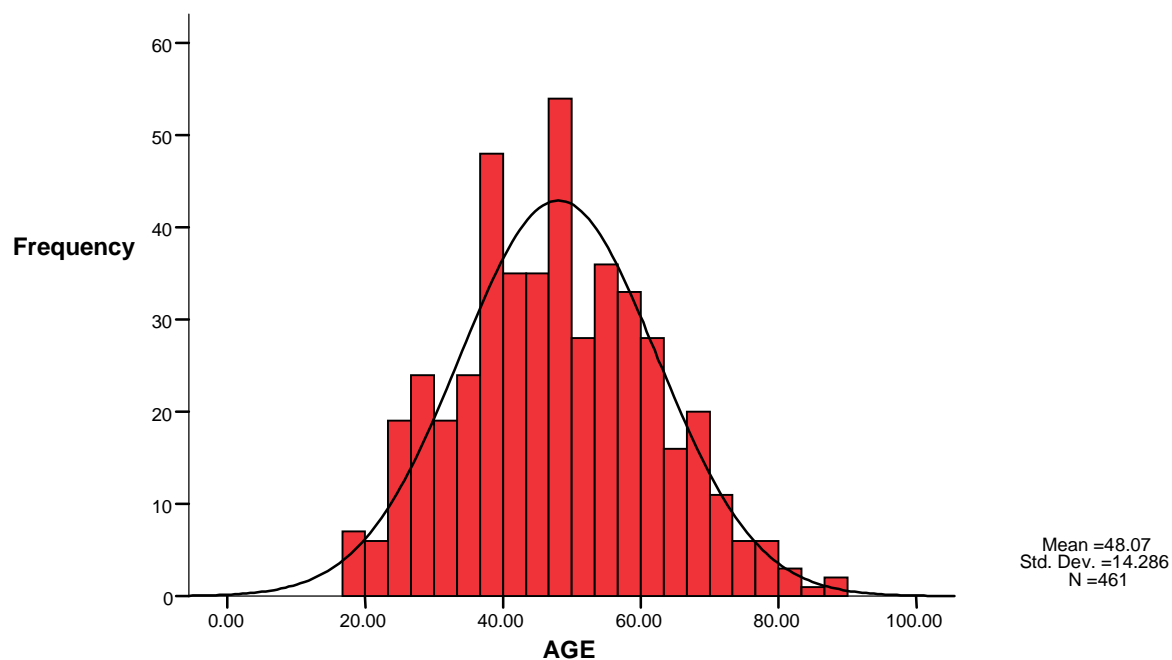
From January 2007 to December 2018, 461 patients underwent surgical thyroid interventions at the surgical Department “A” in Ibn Sina Hospital, Rabat, for different thyroid pathologies. In our series; 291 patients (63.1%) underwent thyroidectomy for Multi nodular goiter, 62 patients (13.4%) for Solitary Nodule, 82 patients (17.8%) for thyroid cancer and 26 patients (5.6%) for Graves’s disease.



**Fig.13** : distribution of patients according to the thyroid pathology diagnosis (n=461).

Women represent 89.2% (411 female patients) versus male patients who represent 10.8% (50 male patients).

In our study the patients’ age varies from a minimum of 18 years old to a maximum of 88 years old, with a mean age of 48 years old (+/- 14.3 years).



**Fig. 14 :** Distribution of patients according to age.

While assessing the patients' health background, we found that in our series 75 patients (16.3%) had hypertension and 38 patients (8.2%) were diabetic.

In addition 74 patients (16.1 %) already underwent surgical interventions in relation with the thyroid gland. Concerning the initial intervention, out of the 74 patients 49 patients (66.2%) underwent a unilateral intervention; 4 of the patients (8.2%) underwent an enucleation and 45 of the patients (91.8%) underwent hemithyroidectomy (4 patients (8.2%) for solitary nodule, 23 patients (46.9%) for multinodular goiter and 22 patients (44.9%) for thyroid cancer).

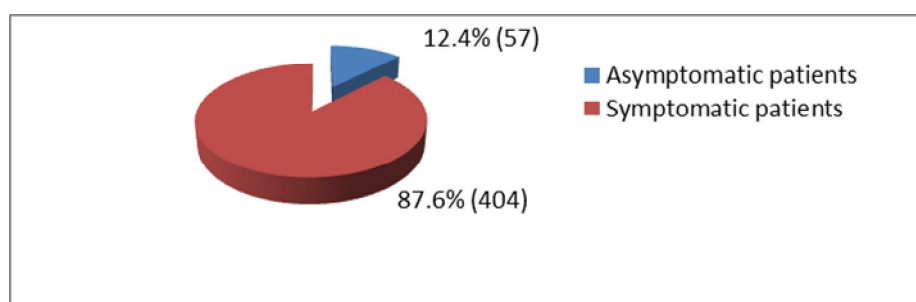
Twenty five patients (33.8%) underwent a bilateral intervention; 7 of the patients (28%) underwent subtotal thyroidectomy and 18 of them patients (72%) underwent total thyroidectomy (22 patients (88%) for thyroid cancer and 3 patients (12%) for multinodular goiter).

## B- Preoperative Clinical, Biochemical And Imaging Tests Features:

### 1- Clinical features:

During admission 57 patients (12.4%) were asymptomatic and 404 patients (87.6%) were symptomatic. The symptoms included; compression signs (dysphonia, dyspagia, dyspnea ), thyroid enlargement causing a lump in the neck, cervical pain, hyperthyroidism signs ( tachycardia nervousness and irritability, heart palpitations, heat intolerance and increased sweating, tremors, weight loss with increase in appetite, frequent bowel movements...) and exophthalmos .

Thus; 256 patients presented cervical tumefaction, 132 patients had compression signs, 50 patients presented cervical pain and 147 patients presented hyperthyroidism signs.



**Fig. 15** : Distribution of patients according to clinical status (n=461).

## 2- Biochemical factors:

All patients got their TSH, calcium and phosphorus measured preoperatively. One hundred and forty three patients (31.0%) with TSH below 0.5mUI/l are considered to have hyperthyroidism and received preoperative treatment until euthyroid status was reached. Three hundred and twelve patients (67.7%) had a TSH within the normal range, and for 6 patients (1.3%) we don't have any information regarding any preoperative biochemical results in their medical dossier.

In addition out of 279 patients, 14 (5%) patients presented preoperative hypocalcaemia (calcemic level <85mg/l), 265 (95%) patients had normal calcemia level. Out of the 14 patients with preoperative hypocalcaemia, 12 (85.7%) were women and 2 (14.3%) were male. Furthermore out of the 14 patients, 8 of them (57.1%) had preoperative hyperthyroidism and 6 of them (42.9%) had normal TSH levels. Concerning the diagnostic 8 patients (57.2%) had MNG, 3 patients (21.4%) had thyroid cancer and 3 patients (21.4%) had solitary nodule.

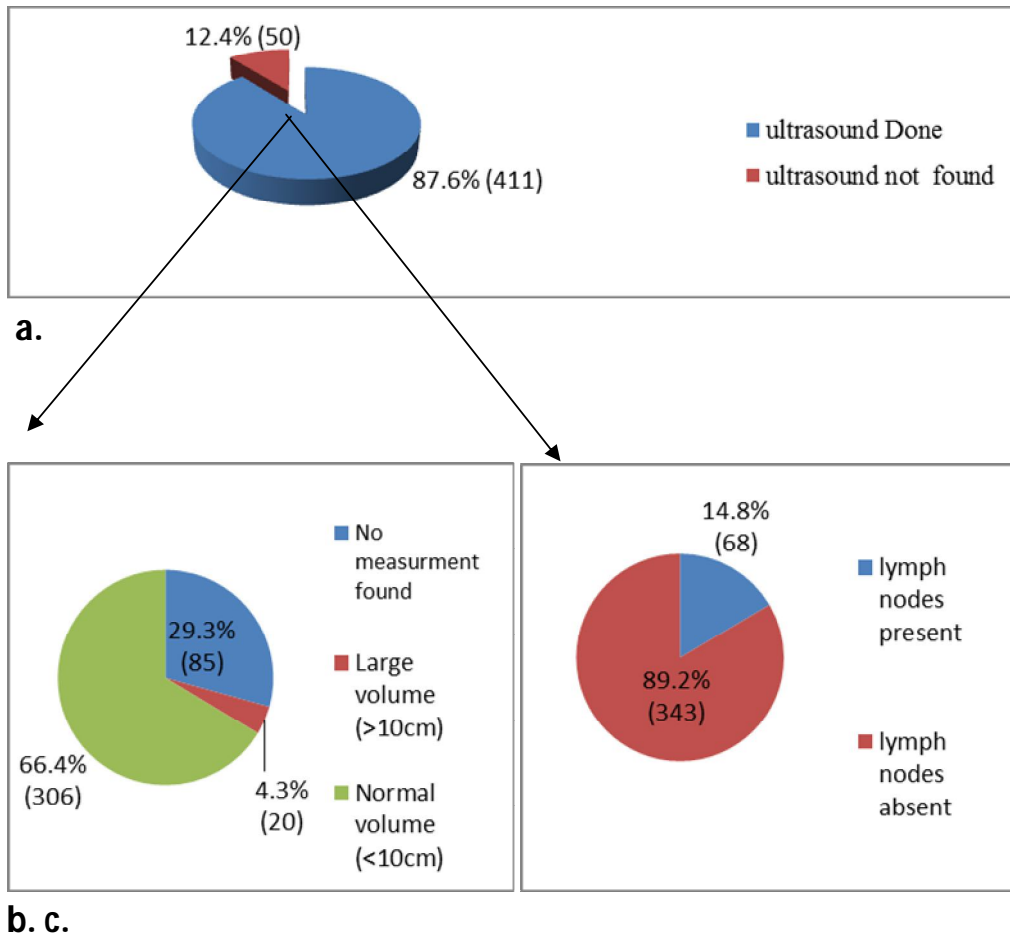
		Preoperative calcemia in mg/l	Preoperative phosphorus in mg/l
N	Valid	280	251
	Missing	181	210
Mean		92.0549	35.0325
Median		92.0000	34.0000
Std. Deviation		5.37465	7.73768
Minimum		62.00	20.00
Maximum		113.00	90.00

**Tab I** : Preoperative calcemia and Phosphorus levels.

### 3- Imaging tests factors:

- **Cervical Ultrasound (US) :**

US were done for 411 patients; 20 patients (4.9%) had a large volume goiter and 306 patients (74.4%) had a normal volume thyroid gland. For 85 patients (20.7%), we do not have any information of the thyroid gland measurements on the US interpretations. Lymph nodes were visible for 68 patients (16.5%).



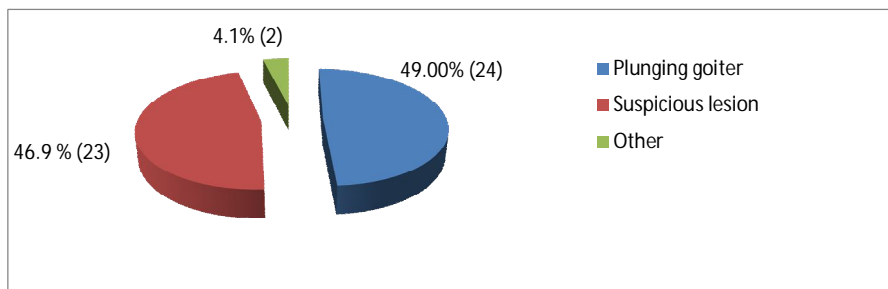
**Fig 16 : a;** Distribution of patients according to ultrasound results (n=461); **b;** thyroid volume (n=411), **c;** Lymph Nodes on ultrasound (n=411).

- **Thoracic Radiology :**

All the patients got systematically a thoracic radiology; 58 patients (12.6%) presented signs of compression (trachea deviation) and 403 (87.4%) patients had normal thoracic radiology.

- **CT scan :**

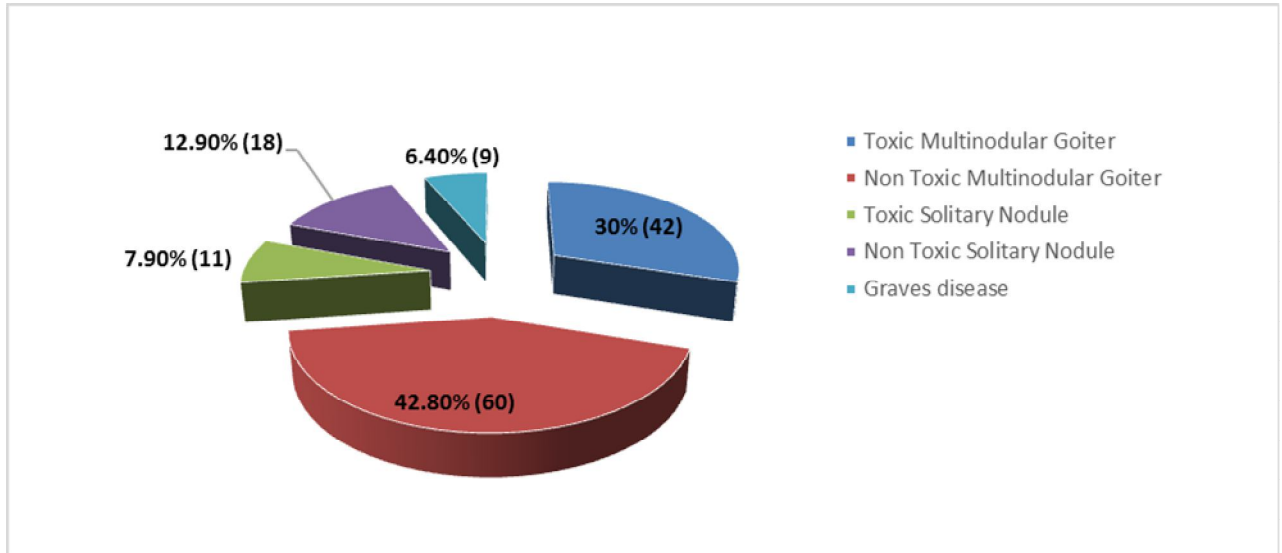
In our study population, 49 patients (10.8%) got a CT scan. Twenty four of them had plunging goiter, 23 of them had suspicious images on US (EU-TIRADS 4, EU-TIRADS 5) and 2 patients presented clinically advanced pathologies.



**Fig 17 :** Distribution of patients according to CT scan results (n=49).

- **Thyroid scintigraphy:**

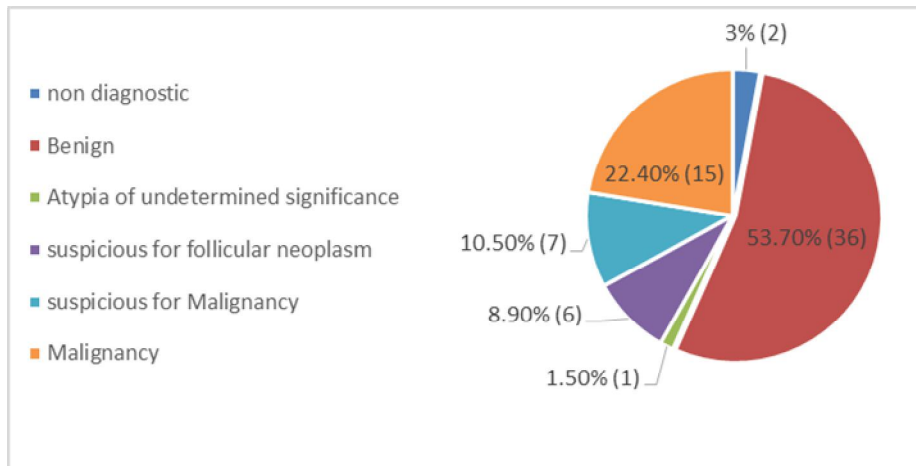
Patients with hyperthyroidism signs with TSH level bellow 0.5mUI/l got a thyroid scintigraphy. Thus 140 patients (30.4%) got a thyroid scintigraphy.



**Fig 18 :** Distribution of patients according to thyroid scintigraphy results (n=140).

#### 4- Cytology tests :

Sixty seven patients (14.6%) patients who had suspicious nodules clinically or/and on imagery (>20mm, euTIRADS4-5) got a FNAB.



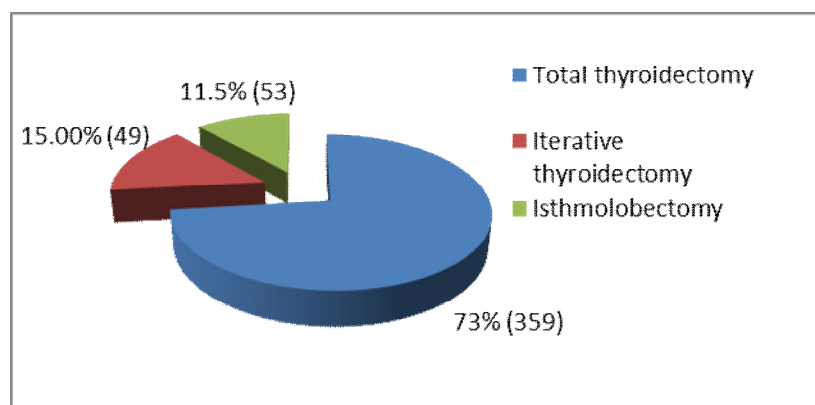
**Fig 19 :** Distribution of patients according to FNAB results (n=67).

#### C- Surgical procedure features :

##### 1- Type of intervention:

For our study we divided our patients into two groups; 1st group includes patients who underwent unilateral intervention (isthmo-lobectomy) which is 53 patients (11.5%). The 2nd group includes patients who underwent bilateral intervention (total thyroidectomy for 359 patients or iterative completion thyroidectomy for 49 patients) which is 408 patients (88.5%).

For patients who already had undergone thyroidectomy prior to this current intervention; 4 out of the 49 patients who underwent unilateral intervention benefited from enucleation; 1 patient got a hemithyroidectomy and the 3 patients underwent totalisation. The rest of the 45 patients who had undergone hemithyroidectomy all underwent totalisation of the previous thyroidectomy. Out of the 25 patients who had undergone bilateral intervention for the iterative intervention, 10 had lymph nodes dissection, 14 patients underwent remnant tissue resection and 1 patient had both lymph nodes dissection and remnant tissue resection.



**Fig 20 :** Distribution of patients according to the type of surgery (n=461).

## 2- Detection of the recurrent nerves :

	Gender	Prior thyroid surgery	Preoperative hyperthyroidism	Diagnosis	Location of the RN	Post-operative dysphonia
<b>Patient 1</b>	Female	Yes	Yes	Thyroid cancer	Right	No
<b>Patient 2</b>	Female	No	Yes	MNG	Left	Yes
<b>Patient 3</b>	Female	No	No	MNG	Right	No
<b>Patient 4</b>	Female	No	No	MNG	Left	No
<b>Patient 5</b>	Female	No	Yes	Thyroid cancer	Right	Yes

**Tab II:** Characteristics of the 5 patients undergoing total thyroidectomy with suspected peroperative lesion of the recurrent nerve.

Out of the 408 patients who underwent bilateral intervention; for 341 patients (83.6%) both recurrent nerves were seen, for 66 patients (16.2%) only 1 recurrent nerve was seen and for 1 patient (0.2%) none of the recurrent nerves were seen. Thus 770 recurrent nerves were dissected and 5 nerves are suspected to have lesion.

Out of the 53 patients who underwent unilateral intervention all 53 recurrent nerves were seen and preserved.

## 3- Parathyroid glands (PTG)

### • PTG Detection

Detection of the parathyroid glands was systematic during intervention, the ideal being 2 or more glands detected.

For the 408 patients undergoing bilateral intervention; 6 patients (1.5%) had none of the PTGs seen during intervention, 25 patients (6.1%) had 1 PTG seen, 75 patients (18.4%) had 2 PTGs seen, 46 patients (11.3%) had 3 PTGs seen and 256 patients (62.7%) had all 4 PTGs seen during surgery. In total 1337 PTGs were seen during intervention.

For patients undergoing unilateral intervention 1 PTG was seen for 11 patients (20.8%) and 2 PTGs were seen for 42 patients (79.2%), thus 95 PTGs were seen.

So in total during the 461 thyroidectomies done in our department 1432 PTGs were seen.

- **Parathyroid incidentaloma :**

Five patients (1.1%) presented parathyroid incidentaloma that was discovered during intervention. The preoperative calcemia mean value for these patients is 97 +/- 7.7 mg/l.

- **Incidental parathyroidectomy and auto-transplantation of PTGs:**

In our study, 33 patients (7.2%) sustained inadvertent parathyroidectomy. In total 36 PTGS were injured, 35 PTGs that were considered viable were transplanted in the sternocleidomastoid muscle. 1 PTG that was intracapsular was not implanted and was found in specimen during anathomopathology examination of the thyroid gland. Out of the 33 patients who benefited from PTGs auto transplantation 2 patients had 2 PTGs each transplanted while 31 of them got 1PTG transplanted. Out of the 2 patients with 2 PTGS implanted 1 patient had symptomatic post-operative hypocalcemia, and both developed transient hypocalcaemia. None of the patient who had PTG auto transplantation developed permanent hypocalcaemia.

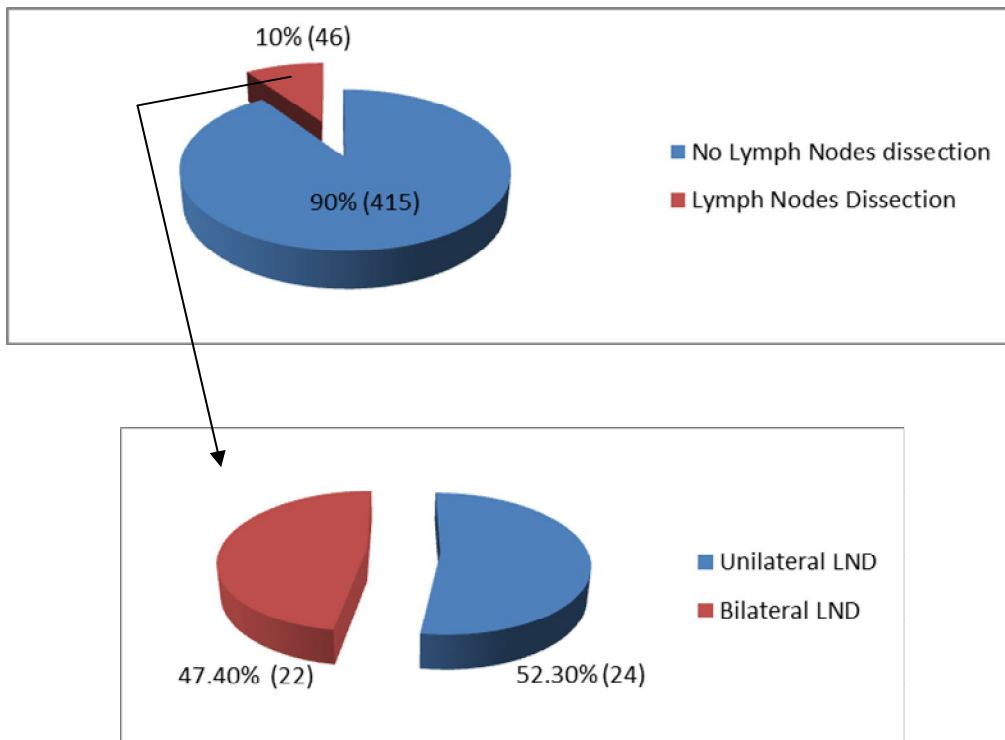
Order of Patient	Type of surgical intervention	Number of PTG seen during surgery	Number of PTG implanted in SCM	Postop Hypocalcemia symptoms	Postop Calcemia status
1	Bilateral Surg	4	1	No	Transient hypocal
2	Bilateral Surg	1	1	Yes	Transient hypocal
3	Bilateral Surg	4	1	No	No hypocal
4	Bilateral Surg	2	1	No	No hypocal
5	Bilateral Surg	3	1	No	Transient hypocal
6	Bilateral Surg	3	1	No	No hypocal
7	Bilateral Surg	3	1	No	No hypocal
8	Unilateral Surg	2	1	No	No Hypocal
9	Bilateral Surg	2	1	No	Transient hypocal
10	Bilateral Surg	4	1	No	No hypocal
11	Bilateral Surg	4	1	No	Transient hypocal
12	Bilateral Surg	2	1	No	No hypocal
13	Bilateral Surg	3	1	No	No hypocal
14	Bilateral Surg	3	1	No	No hypocal
15	Bilateral Surg	2	1	No	No hypocal
16	Bilateral Surg	4	1	No	No hypocal
17	Bilateral Surg	4	1	Yes	Transient hypocal
18	Bilateral Surg	1	1	No	No hypocal
19	Bilateral Surg	2	1	No	No hypocal
20	Bilateral Surg	4	1	No	No hypocal
21	Bilateral Surg	2	2	Yes	Transient hypocal
22	Bilateral Surg	2	1	No	Transient hypocal
23	Bilateral Surg	4	1	Yes	Transient hypocal
24	Bilateral Surg	3	1	No	Transient hypocal
25	Bilateral Surg	1	1	Yes	Transient hypocal
26	Bilateral Surg	3	1	No	Transient hypocal
27	Bilateral Surg	4	1	No	Transient hypocal
28	Bilateral Surg	4	1	No	Transient hypocal
29	Bilateral Surg	4	1	Yes	Transient hypocal
30	Bilateral Surg	4	2	No	Transient hypocal
31	Unilateral Surg	2	1	No	No hypocal
32	Bilateral Surg	4	1	No	No hypocal
33	Bilateral Surg	3	1	Yes	Transient hypocal
<b>TOTAL</b>		97	35		

**Tab III:** PTG detection and auto-transplantation of PTGs.

#### 4- Extent of surgery:

In our study, 46 patients (10%) were eligible for lymph nodes dissection. Out the 46 patients; 31 patients were diagnosed with thyroid cancer prior to intervention, and for 15 patients the decision was taken during surgery (5 of them had solitary nodule and 10 of them had MNG).

Concerning the type neck dissection; 15 patients (32.6%) got a central neck dissection, 22 patients (47.8%) got a posterolateral neck dissection and 9 patients (19.6%) got both anterior and posterolateral dissection.



**Fig 21:** distribution of patients according to the extent of surgery;  
a: Extent of surgery (n=461), b: Bilateral LND *versus* Unilateral LND (n=46).

## 5- Surgical expertise :

The surgical interventions were performed either by a senior surgeon or by residents alone with the supervision of a senior surgeon for teaching purposes. In our series 32 of the interventions (6.9%) were done by residents alone and 429 interventions (93.1%) were performed by the senior surgeons.

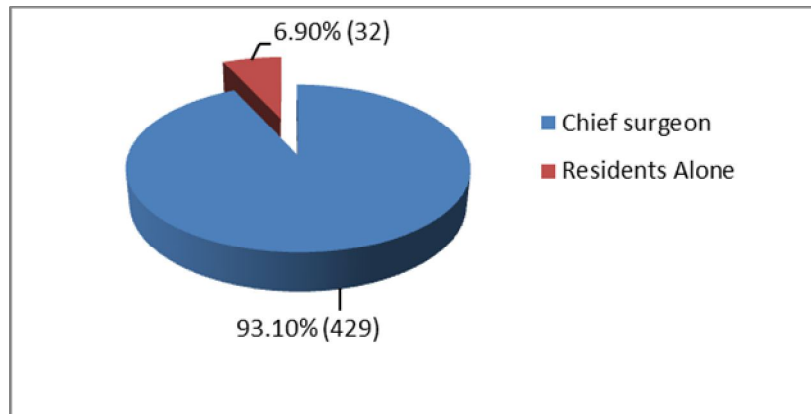


Fig 22: Distribution of patients according to the type of surgery.

## D- Post-operative features:

Post thyroid surgery complications are not uncommon, in our study population there was no deceased patient after intervention but other complication were observed thus we found;

### 1- Hypocalcaemia

In our study 157 patients (34.1%) presented post-operative hypocalcaemia (<80mg/l) and 100 of them (66.9%) received calcium supplementation. Out of the 100 patients who received calcium supplementation treatment 58 patients (58.0%) presented hypocalcaemia symptoms.

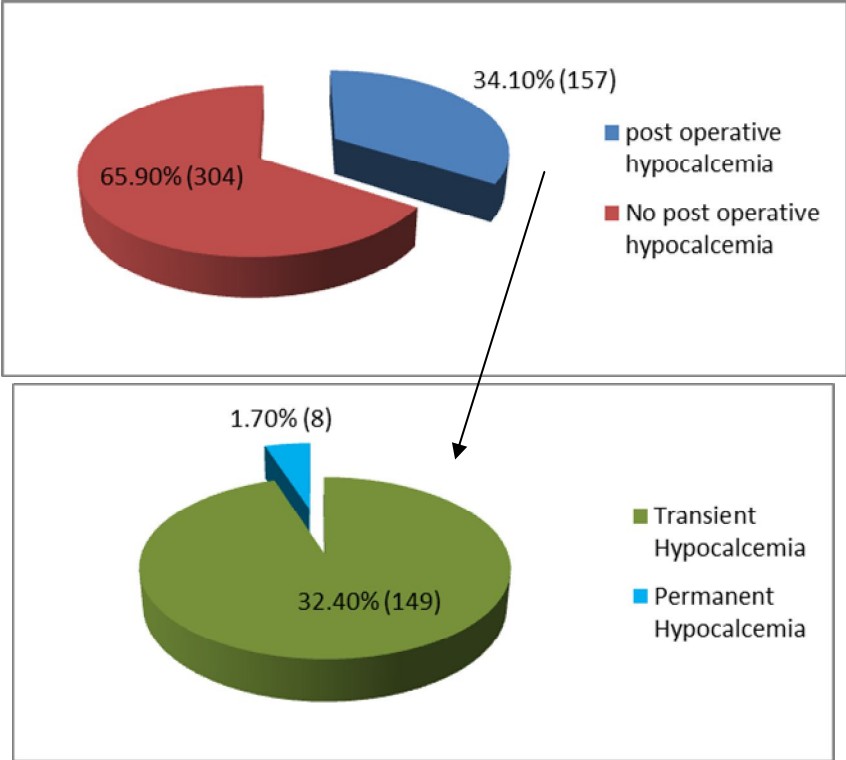
In our series, 149 patients (32.3%) developed a transient hypocalcaemia and 8 patients (1.7%) developed a permanent hypocalcaemia needing calcium supplementation indefinitely. Out of 8, 1 was a male patient and 7 of them were females. All 8 patients with permanent hypocalcaemia were diagnosed with MNG, and 7 of them underwent total thyroidectomy while only 1 patient underwent iterative surgery, none of them had preoperative hypocalcaemia.

## **2- Dysphonia**

Twenty five patients (5.4%) presented post-operative dysphonia, and all 25 received steroid treatments, 10 received vocal cord rehabilitation treatment. All 25 patients (6.3%) developed transient dysphonia and there was no permanent dysphonia.

## **3- Hematomas or hemorrhages**

Ten patients (2.2%) presented post-operative hematomas or hemorrhages that necessitated an emergency surgical reintervention.



**Fig 23:** Post-operative calcemia status (n=461).

## II-UNIVARIATE STATISTICAL ANALYSIS:

### A- Patient and disease related Factors in relations with post thyroidectomy hypocalcaemia and dysphonia:

#### 1-Post thyroidectomy hypocalcaemia :

##### ➤ Age:

For patients who underwent surgical thyroid intervention, the mean age of patients who developed post-operative hypocalcaemia is 48.7 +/- 13.7 years *versus* 47.7 +/- 14.6 years for those who didn't , with  $p = 0.477$ .

The mean age of patients who developed transient hypocalcaemia is 49.2 +/- 13.7 years *versus* 47.5 +/- 14.5 years with those who didn't it is, with  $p= 0.234$ .

The mean age of patients who developed permanent hypocalcaemia is 39.6 +/-9.8 years *versus* 48.2 +/- 14.3 years for those who didn't, with  $p= 0.092$ .

##### ➤ Gender:

We found that 148 of the female patients (36%) *versus* 9 of the male patients (18%) developed post-operative hypocalcaemia, with OR: 2.56, C.I [1.21-5.42] and  $p =0.011$ .

Transient hypocalcaemia was observed in 141 female patients (34.3%) *versus* 8 male patients (16%), with  $p =0.009$ .

In addition permanent hypocalcaemia was observed in 7 female patients (87.5%) *versus* 1 male patient (12.5%), with  $p=0.604$ .

➤ **Antecedent of surgery in connection with thyroid**

In our series post-operative hypocalcaemia was observed for 19 patients (25.7%) that underwent previous thyroidectomy *versus* 138 patients (35.7%) who underwent thyroidectomy for the 1st time, with  $p=0.097$ .

Transient hypocalcaemia was observed in 18 patients (24.3%) that underwent previous thyroidectomy *versus* 131 patients (33.9%) who underwent thyroidectomy for the 1st time, with  $p=0.108$ .

Permanent hypocalcaemia was observed for 1 patients (1.4%) that underwent previous thyroidectomy *versus* 7 patients (1.8%) who underwent thyroidectomy for the 1st time, with  $p=1.000$ .

➤ **Hypertension and Diabetes:**

- **HTA**

On one hand, 21 of the patients (28.0%) who had Hypertension developed post- operative hypocalcaemia *versus* 136 of the patients(35.2%) with no hypertension ,with  $p=0.226$  .

Transient hypocalcaemia was observed in 20 patients (26.7%) that had hypertension *versus* 129 patients (33.4%) who didn't have hypertension , with  $p=0.253$ .

Permanent hypocalcaemia was observed in 1 patient (1.3%) that had hypertension *versus* 7 patients (1.8%) who didn't have hypertension, with  $p=1.000$ .

## - **Diabetes**

On the other hand, 12 patients (31.6%) who had diabetes developed post-operative hypocalcaemia *versus* 145 patients (34.3%) without diabetes, with  $p=0.737$ .

Transient hypocalcaemia was observed in 12 patients (31.6 %) that had diabetes *versus* 137 patients (32.4 %) who didn't have diabetes, with  $p=0.919$ .

Permanent hypocalcaemia was observed in none of the patients that had diabetes *versus* 8 patients (1.9%) who didn't have diabetes, with  $p=1.000$ .

### ➤ **Diagnosis :**

- **Graves disease and Thyroid Cancer *versus* MNG**

We found that 34 patients (31.5%) with either thyroid cancer or Graves' disease developed post thyroidectomy hypocalcaemia *versus* 117 patients (40.2 %) with MNG , with  $p=0.110$ .

Transient hypocalcaemia was observed with 34 patients (31.5%) diagnosed with either thyroid cancer or Graves' disease *versus* 109 patients (37.5%) diagnosed with MNG,  $p=0.269$ .

Permanent hypocalcaemia was observed with none of the patients diagnosed with either thyroid cancer or Graves disease *versus* 8 patients (2.3%) diagnosed with MNG,  $p=0.114$ .

- **Graves disease *versus* other diagnosis**

Post-operative hypocalcaemia was found in 10 patients (38.5%) with Graves disease *versus* 141 patients (37.8%) with other diagnosis, with  $p=0.947$ .

Transient hypocalcaemia was found in 10 patients (38.5%) with Graves disease *versus* 133 patients (35.7%) with other diagnosis, with  $p=0.773$ .

Permanent hypocalcaemia was found in none of patients with Graves disease *versus* 8 patients (2.1%) with other diagnosis, with  $p=1.000$ .

- **Thyroid cancer versus other diagnosis:**

While comparing thyroid cancer *versus* other diagnosis, we found 24 patients diagnosed with thyroid cancer (29.3%) developed post-operative hypocalcaemia *versus* 127 patients (40.1%) patients diagnosed with other thyroid pathology, with  $p=0.072$ .

Transient hypocalcaemia was observed with 24 patients (29.3%) diagnosed with thyroid cancer *versus* 119 patients (37.5%) with other diagnosis, with  $p=0.164$ .

Permanent hypocalcaemia was observed in none of the patients diagnosed with thyroid cancer *versus* 8 patients (2.1%) with other diagnosis, with  $p=0.370$ .

- **MNG versus other diagnosis :**

Post thyroidectomy hypocalcaemia was observed with 117 patients (40.2%) diagnosed with MNG *versus* 34 patients (31.5 %) with other diagnosis, with  $p=0.110$ .

Transient hypocalcaemia was observed with 109 patients (37.5%) diagnosed with MNG *versus* 24 patients (31.5 %) with other diagnosis, with  $p=0.269$ .

Permanent hypocalcaemia was observed with 8 patients (2.7%) diagnosed with MNG while none of the patients with other diagnosis developed permanent hypocalcaemia, with  $p=0.114$ .

➤ **Presence of symptoms pre operatively:**

Concerning preoperative symptoms ; 143 patients (35.4%) that were symptomatic developed hypocalcaemia postoperatively *versus* 14 of the patients (24.6%) that were asymptomatic, with  $p= 0.106$ .

Transient hypocalcaemia was observed with 136 patients (33.7%) that were symptomatic preoperatively *versus* with 13 patients (22.8%) that were asymptomatic, with  $p=0.101$ .

Permanent hypocalcaemia was observed with 7 patients (1.7%) that were symptomatic preoperatively *versus* with 1 patient (1.8%) that were asymptomatic, with  $p=1.000$ .

➤ **Thyroid size on ultrasound :**

In our study we also assessed the relations between thyroid volume on ultrasound (We considered a thyroid volume to be large if at least one measurement  $>10\text{cm}$ ) and the occurrence of hypocalcaemia post operatively.

Thus, we found out of the 20 patients with thyroid volume  $>10\text{cm}$ , 4 patients (20%) developed postoperative hypocalcaemia *versus* 105 patients (34.3%) with normal thyroid volume, with  $p=0.189$ .

Furthermore, out of the 20 patients with thyroid volume  $>10\text{cm}$ , 4 patients (20%) developed transient hypocalcaemia *versus* 98 patients (34.3%) with normal thyroid volume, with  $p=0.261$ .

Permanent hypocalcaemia was observed with none of the patients with thyroid volume  $>10\text{cm}$  while 8 patients (2.3%) with normal thyroid volume developed permanent hypocalcaemia, with  $p=1.000$ .

## **2-Post thyroidectomy dysphonia :**

None of the patients in our series developed permanent dysphonia, thus every patient with post-operative dysphonia recovered before 12 months resulting in transient dysphonia. All post-operative dysphonia are all transient.

### **➤ Age:**

The mean age of patients who developed post-operative dysphonia is 47.7 +/-12.5 years *versus* 48.1 +/- 14.4 years for the patients who didn't develop post thyroidectomy dysphonia ,with  $p=0.887$ .

### **➤ Gender:**

Post thyroidectomy dysphonia was observed with 23 of the female patients (5.6%) *versus* and with 2 of the male patients (4.0%), with  $p=1.000$ .

### **➤ Antecedent of surgery in connection with thyroid:**

Post-operative dysphonia was found in 1 patient (1.4%) that underwent previous thyroidectomy *versus* in 24 patients (6.2%) undergoing thyroidectomy for the 1st time, with  $p=0.749$ .

### **➤ Hypertension and Diabetes:**

On one hand, post-operative dysphonia was observed with 4 patients (5.3%) with hypertension *versus* 21 patients (5.4%) without hypertension, with  $p=1.000$ .

On the other hand, post-operative dysphonia was observed with 2 patients (5.3%) with diabetes *versus* 23 patients (5.4%) without diabetes, with  $p=1.000$ .

➤ **Diagnosis :**

We did not include solitary nodule for comparison as we know all patients diagnosed with solitary nodule underwent hemithyroidectomy, thus n=399 patients.

• **Graves disease and Thyroid Cancer *versus* MNG**

Post-operative dysphonia was observed with 8 patients (7.4%) diagnosed with either thyroid cancer or Graves disease *versus* 16 patients (5.5%) diagnosed with MNG,  $p=0.476$ .

• **Graves disease *versus* other diagnosis**

Two patients (7.7%) with Graves' disease developed post-operative dysphonia *versus* 22 patients (5.9%) with other diagnosis, with  $p=0.664$ .

• **Thyroid cancer *versus* other diagnosis:**

Post-operative dysphonia was observed with 6 patients (7.3%) diagnosed with thyroid cancer *versus* 18 patients (5.7%) with other diagnosis, with  $p=0.603$ .

• **MNG *versus* other diagnosis :**

Post thyroidectomy dysphonia was observed with 16 patients (5.5%) diagnosed with MNG *versus* 8 patients (7.4%) with other diagnosis with  $p=0.476$ .

➤ **Presence of symptoms pre operatively:**

Post-operative dysphonia was observed with 23 patients (5.7%) that were symptomatic preoperatively as against 2 patients (3.5%) that were asymptomatic, with  $p=0.755$ .

➤ **Thyroid size on ultrasound :**

Post-operative dysphonia was observed in 3 patients (15.0%) with large volume goiter *versus* 17 patients (5.6%) with normal thyroid volume,  $p=0.115$ .

Variables	N=461 %(n)	Postop	p value	Postop	p value
		hypocalcemia 34.1%(n=157)		dysphonia 5.4% (n=25)	
<b>Age,years (mean +/- SD)</b>	47.7 +/- 14.6	48.7 +/-13.7	0.477	47.7 +/- 12.5	0.887
<b>Gender</b>			0.011		1.000
Male (%)	10.8%(50)	18% (9)		4% (2)	
Female (%)	89.2%(411)	36% (148)		5.6% (23)	
<b>ATD thyroid surgery</b>			0.097		0.749
Yes	16.1% (74)	25.7% (19)		1.4% (1)	
No	83.9% (387)	35.7% (138)		6.2% (24)	
<b>HTA</b>			0.226		1.000
Yes	16.3% (75)	28.0% (21)		5.3% (4)	
No	83.7% (386)	35.2% (136)		5.4% (21)	
<b>Diabetes</b>			0.737		1.000
Yes	8.2% (38)	31.6% (12)		5.3% (2)	
No	91.8% (423)	34.3% (145)		5.4% (23)	
<b>Diagnosis :Thyroid cancer vs Other</b>			0.072		0.603
Thyroid cancer	20.6% (82)	27.1% (108)		7.3% (6)	
Other	79.4 % (317)	40.1% (127)		5.7% (18)	
<b>Preoperative clinical symptoms</b>			0.106		0.755
Symptomatic	87.6% (404)	35.4% (143)		5.7% (23)	
Asymptomatic	12.4% (57)	24.6% (14)		3.5% (2)	
<b>Thyroid volume</b>			0.261		0.115
>10 cm	4.9% (20)	20% (4)		15.0% (3)	
<10 cm	74.4% (306)	34.3% (105)		5.6% (17)	

**Tab IV:** Patient and disease related Factors in relations with post-operative hypocalcaemia and dysphonia.

Variables	N=461 % (n)	Transient hypocalcemia n=149 (32.3%)	P value	Permanent hypocalcemia n=8 (1.7%)	P value
<b>Age,years (mean +/- SD)</b>	47.7 +/- 14.6	49.2 (+/-13.7)	0.234	39.6 (+/-9.8)	0.092
<b>Gender</b>			0.009		0.604
Male (%)	10.8%(50)	16% (8)		87.5% (7)	
Female (%)	89.2%(411)	34.3% 141		12.5% (1)	
<b>ATD thyroid surgery</b>			0.108		1.000
Yes	16.1% (74)	24.3% (18)		1.4% (1)	
No	83.9% (387)	33.9% (131)		1.8% (7)	
<b>HTA</b>			0.253		1.000
Yes	16.3% (75)	26.7% (20)		1.3% (1)	
No	83.7% (386)	33.4% (129)		1.8% (7)	
<b>Diabetes</b>			0.919		1.000
Yes	8.2% (38)	31.6% (12)		0% (0)	
No	91.8% (423)	32.4% (137)		1.9% (8)	
<b>Diagnosis :Thyroid cancer Vs Other</b>			0.164		0.370
Thyroid cancer	20.6% (82)	29.3% (24)		0 % (0)	
Other	79.4 % (317)	37.5% (125)		2.1% (8)	
<b>Preoperative clinical symptoms</b>			0.101		1.000
Symptomatic	87.6% (404)	33.7% (136)		1.7% (7)	
Asymptomatic	12.4% (57)	22.8% (13)		1.8% (1)	
<b>Thyroid volume</b>			0.261		1.000
>10 cm	4.9% (20)	20% (4)		0% (0)	
<10 cm	74.4% (306)	32.0% (98)		2.3% (7)	

**Tab V:** Patient and disease related Factors in relations with post thyroidectomy, transient and permanent hypocalcaemia.

## **B- Pre-operative Biochemical related factors associated with post thyroidectomy hypocalcaemia and dysphonia**

### **1- Post thyroidectomy hypocalcaemia :**

#### **➤ TSHus,T3 and T4:**

In our study, post thyroidectomy hypocalcaemia was observed in 58 patients (40.6%) who had preoperative hyperthyroidism *versus* 99 patients (31.7%) with normal TSH level, with  $p=0.066$ .

Transient hypocalcaemia was observed in 57 patients (39.9%) who had preoperative hyperthyroidism *versus* 92 patients (29.5%) with normal TSH level, with  $p=0.029$ .

Permanent hypocalcaemia was observed in 1 patient (7.0%) who had preoperative hyperthyroidism *versus* 7 patients (2.2%) with normal TSH level, with  $p=0.445$ .

#### **➤ Calcium and Phosphorus levels**

We found that 14 patients have pre-operative hypocalcaemia (<85mg/l); 12 of them were females and the 2 patients are males, 3 of them had already underwent thyroid surgery, 5 of them presented preoperative hyperthyroidism. The mean age of the patients with preoperative hypocalcaemia is 50.6 years +/- 14.7 *versus* those with normal calcemia level is 47.5 years +/- 14.3, with  $p=0.430$ .

Out of the 14 patients, 11 (78.6%) of them developed post-operative hypocalcaemia *versus* 87 patients (32.8%) who developed post-operative hypocalcaemia without pre-operative hypocalcaemia, with  $p=0.001$ .

Transient hypocalcaemia was observed in 11 patients (78.6%) who had preoperative hypocalcaemia *versus* 82 patients (30.9%) with normal preoperative calcemia level, with  $p=0.001$ .

Permanent hypocalcaemia was observed in none of the patients who had preoperative hypocalcaemia while 5 patients (1.9%) with normal preoperative calcemia level, with  $p=1.000$ .

	No Tansient hypocal	Transient hypocal	<i>p</i> value	No permanent hypocal	Permanent hypocal	<i>p</i> value
<b>Preop calcemia *</b>	93.1+/-4.58	90.1+/-6.32	<0.001	92.0+/-5.39	92.2+/-6.87	0.965
<b>Ca postop Day 1 *</b>	86.0+/-5.24	74.4+/-5.31	<0.001	82.1+/-7.6	74.6+/-6.6	0.006
<b>Ca postop Day 2 *</b>	87.6+/-6.01	73.7+/-6.56	<0.001	82.52+/-9.09	69.8+/-2.9	<0.001
<b>Preop phosphorus *</b>	35.3+/-7.16	34.5+/-8.76	0.459	35.0+/-7.77	37.4+/-4.16	0.486
<b>P postop Day 1 *</b>	33.0+/-6.96	38.5+/-9.61	<0.001	34.7+/-8.23	45.5+/-10.18	<0.001
<b>P postop Day 2 *</b>	47.5+/-14.53	49.2+/-14.53	0.234	34.6+/-8.55	44.9+/-20.22	0.002

\*Mean in mg/l +/- SD

**Tab VI:** Preoperative and post-operative Calcemia and Phosphorus level for patients with and without transient hypocalcaemia.

## 2- Post thyroidectomy Dysphonia :

### ➤ TSHus,T3 and T4:

Eight patients (5.6%) with pre-operative hyperthyroidism *versus* 17 patients (5.4%) with normal TSH level developed post-operative, with  $p=0.950$ .

### ➤ Calcium and Phosphorus levels

Post-operative dysphonia was observed in 1 patient (7.1%) with pre-operative hypocalcaemia *versus* 13 patients (4.69%) without pre-operative hypocalcaemia with  $p=0.522$ .

variables	N=461 % (n)	Hypocal Postop	<i>p</i> value	Transient hypocal	<i>p</i> value	Permanent hypocal	<i>p</i> value	Postop dysphonia	<i>p</i> value
Preoperative hyperthyroidism			0.066		0.029		0.445		0.950
Yes	31.4% (143)	40.6% (58)		39.9% (57)		7% (1)		5.6% (8)	
No	68.6% (312)	31.7% (99)		29.5% (92)		2.2% (7)		5.4% (17)	
Pre-operative hypocalcaemia			0.001		0.001		1.000		0.522
Yes	5% (14)	78.6% (11)		78.6%(11)		0% (0)		7.1% ( 1)	
No	95% (265)	32.8% (87)		30.9%(82)		1.9% (5)		4.69% (13)	

**Tab VII:** Pre-operative Biochemical related Factors associated with post thyroidectomy, Transient and permanent hypocalcaemia and post thyroidectomy dysphonia.

## **C- Surgical factors associated with post thyroidectomy hypocalcaemia and post-operative dysphonia :**

### **1- Post thyroidectomy hypocalcaemia :**

#### **➤ Type of intervention :**

The 1st group includes patients who got a unilateral intervention which is 58 patients; 2 patients (3.8%) developed post-operative hypocalcaemia, *versus* 155 patients (38%) from the second group who underwent bilateral intervention, with  $p=0.000$ .

Transient hypocalcaemia was observed in 147 of the patients (36.0%) that underwent bilateral intervention *versus* 2 patients (3.8%) that underwent unilateral intervention, with  $p=0.000$ .

Permanent hypocalcaemia was observed in 8 of the patients (2.0%) that underwent bilateral intervention while none of the patients that underwent unilateral intervention developed permanent hypocalcaemia, with  $p=0.605$ .

#### **➤ Parathyroid Glands :**

##### **• PTGs detection**

In our study 408 patients (88.5%) underwent bilateral intervention. Out of the 377 patients who had 2 or more PTGs seen during intervention, 144 patients (38.2%) developed post-operative hypocalcaemia *versus* 11 patients (35.5%) out of the 31 patients who had less than 2 PTGs seen during intervention, with  $p=0.765$ .

Out of the 377 patients who had 2 or more PTGs seen during intervention 137 patients (36.3%) developed transient hypocalcaemia *versus* 10 patients (32.3%) out of the 31 patients who had less than 2 PTGs seen during intervention, with  $p=0.649$ . Permanent hypocalcaemia was observed in 7 patients (1.9%) who had 2 or more PTGs seen during intervention *versus* 1 patient (3.2%) who had less than 2 PTGs seen during surgery, with  $p=0.472$ .

Concerning the 53 patients (11.5%) that underwent unilateral intervention; 1 patient out the 42 patients who had both PTGs seen developed a post-operative hypocalcaemia *versus* 1 patient out of the 11 patients who had only 1 PTG seen during surgery, with  $p=0.375$ . Transient hypocalcaemia was observed in 1 patient (2.4%) who had both PTGs seen during intervention *versus* 1 patient (9.1%) who had 1 PTGs seen during surgery, with  $p=0.375$ . None of the patients that underwent unilateral intervention developed permanent hypocalcaemia.

- **Parathyroid incidentaloma:**

Out of the 5 patients who had parathyroid incidentaloma, 4 patients (80%) developed post-operative hypocalcaemia *versus* 153 patients (33.6%) out of 456 without it, with  $p=0.048$ .

Transient hypocalcaemia was observed with 3 patients (60%) with parathyroid incidentaloma *versus* 146 patients (32.0%) without it, with  $p=0.335$ .

Permanent hypocalcaemia was observed with 1 patient (20.0%) with parathyroid incidentaloma *versus* 7 patients (1.5%) without it, with  $p=0.084$ .

- **Inadvertent Parathyroidectomy and auto-implantation of PTGs :**

Out of the 36 patients who sustained inadvertent parathyroidectomy 18 patients (50%) developed post-operative hypocalcaemia *versus* 139 patients (32.7%) without accidental removal of the PTGs, with  $p=0.036$ . Post-operative hypocalcaemia was observed in the 17 patients (51.5%) out of the 33 patients who benefited of PTG auto transplantation *versus* 140 patients (32.7%) who didn't, with  $p=0.028$ .

Transient hypocalcaemia was observed with 18 patients (50%) with incidental parathyroidectomy *versus* 131 patients (30.8%) without it, with  $p=0.018$ . And 17 patients (51.5%) with PTG transplantation developed transient hypocalcaemia *versus* 132 patients (30.8%) who didn't, with  $p=0,014$ .

None of the patients with incidental parathyroidectomy developed permanent hypocalcaemia while 8 patients (1.9%) without it did, with  $p=1.000$ . The same result was found for patients who received PTGs transplantations.

We assessed the preoperative and post-operative calcemic level of the 5 patients with parathyroid incidentaloma *versus* patients without it and calcium levels before and after thyroidectomy for patients who benefited from PTGs transplantation *versus* patients who didn't;

	Parathyroid incidentaloma a	No Parathyroid incidentaloma	<i>p</i> value	PTGs auto-implantation	No PTGs auto-implantation	<i>p</i> value
<b>Preop calcemia *</b>	97.1 +/-7.7	92.0 +/-5.3	0.037	91.2 +/-5.56	92.1 +/-3.24	0.402
<b>Ca postop Day 1 *</b>	78.2 +/-3.9	82.0 +/-7.7	0.265	78.9 +/-8.29	82.2 +/-7.55	0.019
<b>Ca postop Day 2 *</b>	75.0 +/-6.7	82.3 +/-9.2	0.078	78.6 +/-9.6	82.5 +/-9.1	0.034
<b>Preop phosphorus *</b>	32.8 +/-3.0	35.1 +/-7.8	0.518	33.9 +/-5.26	35.1 +/-7.91	0.571
<b>P postop Day 1 *</b>	41.0 +/-12.7	34.8 +/-8.3	0.104	34.7 +/-6.76	34.9 +/-8.53	0.896
<b>P postop Day 2 *</b>	48.4 +/-21.1	34.6 +/-8.7	0.001	33.9 +/-7.06	34.9 +/-9.34	0.571

\*Mean in mg/l +/- SD

**Tab VIII:** Preoperative and post-operative Calcemia and Phosphorus level for patients with and without parathyroid incidentaloma and patients with and without PTGs auto implantations.

➤ **Recurrent nerves :**

Out of the 5 patients who are suspected to have lesion of a recurrent nerves 3 (60%) of them developed post-operative hypocalcaemia *versus* 154 patients (33.8%) out of the 456 patients who had no lesion of any of the recurrent nerves during surgery, with  $p= 0.343$ .

Transient hypocalcaemia was observed in 3 patients (60.0%) who had suspected lesion of the recurrent nerve *versus* 146 patients (32.0%) who had no lesion of the recurrent nerve, with  $p=0.335$

Permanent hypocalcaemia was observed in none of the patients who had suspected lesion of the recurrent nerve *versus* 8 patients (1.8%) who had no lesion of the recurrent nerve, with  $p=1.000$ .

➤ **Extent of surgery :**

• **Central neck dissection *versus* Postero-lateral neck dissection**

Post-operative hypocalcaemia was observed with 8 patients (33.3%) out of the 24 patients who got a central neck dissection *versus* with 8 patients (36.4%) out of the 22 patients who underwent postero-lateral neck dissections, with  $p=0.829$ .

Transient hypocalcaemia was observed with 8 patients (33.3%) who got a central neck dissection *versus* with 8 patients (36.4%) who underwent postero-lateral neck dissections, with  $p= 0.829$ .

None of the patients who underwent neck dissection developed permanent hypocalcaemia.

• **Unilateral neck dissection *versus* Bilateral neck dissection**

Eleven patients (50%) out of out of the 22 patients who underwent bilateral neck dissection developed post-operative hypocalcaemia while 5 patients (20.8%) out of the 24 patients who underwent unilateral neck dissection developed post-operative hypocalcaemia, with  $p=0.038$  .

Transient hypocalcaemia was observed with 11 patients (50.0%) who got a bilateral neck dissection *versus* with 5 patients (20.8%) who underwent unilateral neck dissections, with  $p= 0.038$ .

None of the patients who underwent neck dissection developed permanent hypocalcaemia.

➤ **Surgical expertise :**

Out the 32 surgical interventions performed by the residents alone while being supervised by a chief surgeon 8 patients (25.0%) developed a post-operative hypocalcaemia *versus* 149 patients (34.7%) whose surgeries were performed by the chief surgeons, with  $p=0.262$ .

Transient hypocalcaemia was observed with 7 patients (21.9%) whose surgeries were performed by the residents alone while being supervised by a chief surgeon *versus* 142 patients (33.1%) whose surgeries were performed by the chief surgeons, with  $p=0.190$ .

Permanent hypocalcaemia was observed with 1 patient (3.1%) whose surgeries were performed by the residents alone while being supervised by a chief surgeon *versus* 7 patients (1.6%) whose surgeries were performed by the chief surgeons, with  $p=0.440$ .

**2- Post thyroidectomy Dysphonia :**

None of the patients developed permanent dysphonia so all post-operative dysphonia was transient.

➤ **Type of intervention :**

Post-operative dysphonia was observed in 24 of the patients (5.9%) that underwent bilateral intervention *versus* 1 patient (1.9%) that underwent unilateral intervention, with  $p=0.339$ .

➤ **Parathyroid Glands :**

• **PTGs detection :**

For patient that underwent bilateral intervention post-operative dysphonia was observed in 22 patients (5.8%) who had 2 or more PTGs seen during surgery *versus* 2 patients (6.5%) who had less than 2 PTGs seen, with  $P=0.702$ .

For patients who underwent unilateral intervention post-operative dysphonia was observed with 1 patient (9.1%) who had 1 PTG seen *versus* 0 patient with both PTGs seen during intervention, with  $p=0.208$ .

• **Parathyroid incidentaloma:**

Out of the 5 patients who had parathyroid incidentaloma 1 patient (20%) developed post-operative dysphonia *versus* 24 patients (5.3%) out of 456 without it, with  $p=0.244$ .

• **Inadvertent parathyroidectomy and auto-transplantation of PTGs:**

Out of the 36 patients who sustained inadvertent parathyroidectomy, 3 patients (8.3%) developed post-operative dysphonia *versus* 22 patients (5.2%) without accidental removal of the PTGs, with  $p=0.432$ . Post-operative dysphonia was observed in 2 patients (6.1%) out of the 33 patients who benefited of PTG auto implantation *versus* 23 patients (5.4%) who didn't, with  $p=0.697$ .

➤ **Recurrent nerves :**

Post-operative dysphonia was observed with 2 patients (40%) who had suspected peroperative lesion of the recurrent nerve *versus* 23 patients (5.0%) with no lesion of any of the recurrent nerves during surgery, with  $p=0.026$ .

➤ **Extent of surgery :**

• **Central neck dissection *versus* Postero-lateral neck dissection:**

Post-operative dysphonia was observed with 1 patient out of the 24 patients who got a central neck dissection *versus* 1 patient out of the out of 22 patients who underwent postero-lateral neck dissections, with  $p= 1.000$ .

• **Unilateral neck dissection *versus* Bilateral neck dissection**

Post-operative dysphonia was observed with 1 patient out of the 24 patients who got a central neck dissection *versus* with 1 patient out of the Out of the 22 patients who underwent postero-lateral neck dissections, with  $p= 1.000$ .

➤ **Surgical expertise :**

Post-operative dysphonia was observed with none of the 32 patients whose surgery were performed by residents under supervision while 25 patients (5.8%) out of 429 patients whose surgeries were performed by chief surgeons developed post-operative dysphonia, with  $p=0.243$ .

Variables	N=461 % (n)	Postoperative Hypocal	P value	Postoperative Dysphonia	P value
<b>Type of intervention</b>			0.000		0.339
Bilateral	88.5% (408)	38.0% (155)		5.9% (24)	
Unilateral	11.5% (53)	3.8% (2)		1.9% (1)	
<b>Bilateral intervention:</b>			0.765		0.702
2 or more PTGs seen	92.4% (377)	38.2% (144)		5.8% (22)	
<2 PTGs seen	7.6% (31)	35.5% (11)		6.5% (2)	
<b>Unilateral intervention:</b>			0.375		0.208
Both PTGs seen	79.2% (42)	2.4% (1)		0% (0)	
1 PTG seen	20.8% (11)	9.1% (1)		9.1% (1)	
<b>Inadvertant parathyroidectomy</b>			0.036		0.432
Yes	7.8% (36)	50% (18)		8.3% (3)	
No	92.2% (425)	32.7% (139)		5.2% (22)	
<b>PTGs auto-implantation</b>			0.028		0.697
Yes	7.2% (33)	51.5% (17)		6.1% (2)	
No	92.8% (428)	32.7% (140)		5.4% (23)	
<b>Parathyroid incidentaloma</b>			0.048		0.244
Yes	1.1% (5)	80% (4)		20% (1)	
<b>No</b>	98.9% (456)	33.6% (153)		5.3% (24)	
<b>Suspected Lesion of the recurrent nerve</b>			0.343		0.026
Lesion suspected	1.1% (5)	60% (3)		40% (2)	
No Lesion suspected	98.9% (456)	33.8% (154)		5.0% (23)	
<b>Central neck dissection VS Postero-lateral neck dissection</b>			0.829		1.000
CND	52.2% (24)	33.3% (8)		4.2% (1)	
LND	47.8% (22)	36.4% (8)		4.5% (1)	
<b>Bilateral neck dissection Vs Unilateral dissection</b>			0.038		1.000
Bilateral ND	47.8% (22)	50% (11)		4.5% (1)	
Unilateral ND	52.2% (24)	20.8% (5)		4.2% (1)	
<b>Surgical expertise</b>			0.262		0.243
Residents	6.9% (32)	25.0% (8)		0% (0)	
Senior surgeon	93.1% (429)	34.7% (149)		5.8% (25)	

**Tab IX:** Surgical Factors associated post-operative hypocalcaemia and dysphonia.

Variables	N=461 % (n)	Transient Hypocal	P value	Permanent Hypocal	P value
<b>Type of intervention</b>			0.000		0.605
Bilateral	88.5% (408)	36.0% (147)		1.96% (8)	
Unilateral	11.5% (53)	3.8% (2)		0% (0)	
<b>Bilateral intervention:</b>			0.649		0.472
2 or more PTGs seen	92.4% (377)	36.3% (137)		1.9% (7)	
<2 PTGs seen	7.6% (31)	32.3% (10)		3.2% (1)	
<b>Unilateral intervention:</b>			0.375		
Both PTGs seen	79.2% (42)	2.4% (1)		0	
1 PTG seen	20.8% (11)	9.1% (1)		0	
<b>Inadvertant parathyroidectomy</b>			0.018		1.000
Yes	7.8% (36)	50% (18)		0% (0)	
No	92.2% (425)	30.8% (131)		1.9% (8)	
<b>PTGs auto-implantation</b>			0.014		1.000
Yes	7.2% (33)	51.5% (17)		0% (0)	
No	92.8% (428)	30.8% (132)		1.9% (8)	
<b>Parathyroid incidentaloma</b>			0.335		0.084
Yes	1.1% (5)	60% (3)		20% (1)	
No	98.9% (456)	32.0% (146)		1.5% (7)	
<b>Suspected Lesion of the recurrent nerve</b>			0.335		1.000
Lesion suspected	1.1% (5)	60% (3)		0% (0)	
No Lesion suspected	98.9% (456)	32.0% (146)		1.8% (8)	
<b>Central neck dissection vs Posterolateral neck dissection</b>			0.829		
CND	52.2% (24)	33.3% (8)		0	
LND	47.8% (22)	36.4% (8)		0	
<b>Bilateral neck dissection vs Unilateral dissection</b>			0.038		
Bilateral ND	47.8% (22)	50% (11)		0	
Unilateral ND	52.2% (24)	20.8% (5)		0	
<b>Surgical expertise</b>			0.190		0.440
Residents	6.9% (32)	21.9% (7)		3.1% (1)	
Senior surgeon	93.1% (429)	33.1% (142)		1.6% (7)	

**Tab X:** Surgical Factors associated with transient and permanent hypocalcaemia.

## D- Post-operative Factors associated with post thyroidectomy hypocalcaemia

### 1- Post-thyroidectomy hypocalcaemia:

#### ➤ Relative changes in post-operative serum and calcium levels :

	Postop Day 1	Postop Day 2	P value
Calcemia in mg/l	81.2 +/-7.56	82.2 +/- 9.22	0.001
Phosphorus in mg/l	35.6 +/-8.95	35.0 +/-9.21	0.196

Tab XI: Post-operative calcemia and phosphorus level.

#### ➤ Post thyroidectomy hematomas and hemorrhage that needed surgical re-intervention :

Out of the 10 patients who needed emergency reintervention, 6 of them (60%) developed post-operative hypocalcaemia after the 2nd emergency reintervention *versus* 151 patients (33.5%) who didn't go under any other reintervention ,with  $p=0.097$ .

Transient hypocalcaemia was observed in 6 patients (60.0%) who underwent the 2nd emergency reintervention *versus* 143 patients (31.7%) who didn't go under any other reintervention, with  $p=0.084$ .

None of the patients developed permanent hypocalcaemia

### 2- Post thyroidectomy dysphonia :

#### ➤ Post thyroidectomy hematomas and hemorrhage that needed surgical re-intervention :

Transient dysphonia was observed with 2 patients (20%) out of the 10 patients who underwent surgical re-intervention *versus* 23 patients (5.1%) out of 451 patients who didn't, with  $p=0.097$ .

### III- MULTIVARIATE STATISTICAL ANALYSIS:

#### 1. Post-operative hypocalcaemia :

In the current study for the multivariate analysis, we assessed 4 variables that were significant in the development of post-operative hypocalcaemia in the univariate analysis, thus we tested gender ( $p=0.009$ ), preoperative hypocalcaemia ( $p= 0.001$ ), preoperative hyperthyroidism ( $p=0.066$ ) and type of intervention; unilateral intervention *versus* bilateral interventions ( $p=0.000$ ).

Variables	<i>p</i> value	O.R	C I 95 %
Gender (female)	0.047	2.87	[1.01-8.15]
Preoperative hypocalcemia	0.001	22.21	[3.58-137.72]
Preoperative hyperthyroidism	0.807	1.07	[0.61-1.89]
Bilateral intervention	0.002	15.66	[2.81-87.27]

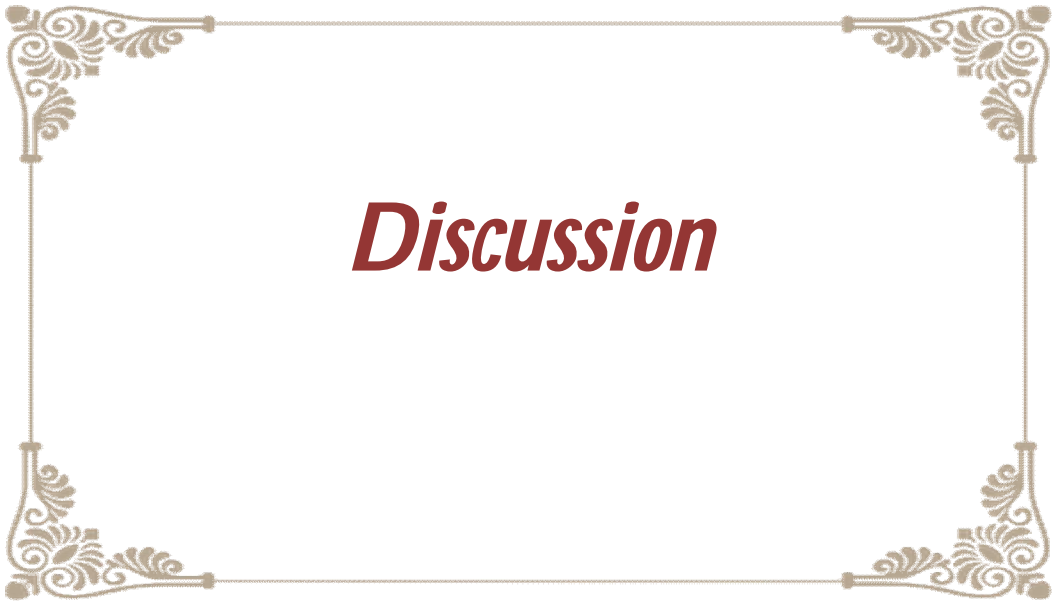
**Tab XII:** Multivariate analysis of factors that affecting to the development of post thyroidectomy hypocalcaemia.

#### 2. Post-operative dysphonia :

We assessed 2 variables; suspected peroperative lesion of the recurrent nerve which was significant on univariate analysis ( $p= 0.026$ ) and large Thyroid size on US ( $p=0.115$ ).

Variables	P value	O.R	C I 95 %
Suspected lesion of the recurrent nerve	0.178	5.69	[0.452-71.622]
Large thyroid size on US	0.164	2.64	[0.673-10.375]

**Tab XIII:** Multivariate analysis of factors that affecting to the development of post thyroidectomy dysphonia.



***Discussion***

## I-POST OPERATIVE HYPOCALCAEMIA:

In the current study; female gender, preoperative hyperthyroidism, preoperative hypocalcaemia, bilateral intervention, bilateral lymph node dissection and inadvertent parathyroidectomy were variables that were significant in a univariate analysis. However in our multivariate analysis only gender, bilateral intervention and preoperative hypocalcaemia were independent significant factors in the development of post thyroidectomy hypocalcaemia.

On the other note variables that were significant in other studies were not significant in the present study. These included; old age, Graves disease, thyroid cancer, number of PTGs detected, central neck dissection, surgical expertise and thyroid volume.

In addition we found that hypertension and diabetes were also none significant variables.

Many studies have evaluated the possible risk factors for post-thyroidectomy hypocalcaemia, some of which have been generally accepted. However, establishing these risk factors continues to be a challenge. In our study, we assessed biological, clinical and surgical factors that may influence the development of post thyroidectomy hypocalcaemia.

In our series 34.1% of the patients developed post-operative hypocalcaemia. 32.3% of them showed recovery before 12 months (transient hypocalcaemia), without the need of replacement therapy for at least 1 month while 1.8% of them needed to maintain calcium supplementation for more than 12 months after surgery (permanent hypocalcaemia). The British Association of Endocrine and Thyroid Surgeons audit [69] reported rates of 27.4 % and 12.1 %

for transient and permanent post-thyroidectomy hypocalcaemia respectively depending on the definition and criteria used to determine transient and permanent hypocalcaemia. The reported rate of post-operative hypocalcaemia varies from one study to another due to a lack of consensus on the definition and criteria of post-operative hypocalcaemia [70]. A meta-analysis of 115 studies [71] found that the biochemical thresholds used to diagnose hypocalcaemia ranged across studies: total calcium 1.88–2.13 mmol/l, corrected calcium 1.70–2.20 mmol/l and serum calcium 1.75–2.25 mmol/l. Some protocols required the presence of clinical symptoms and low levels of hypocalcaemia for the diagnosis, whereas others used either of the two. The time limit used to define long-term hypocalcaemia after surgery ranged from 3 months to 2 years.

#### ❖ Gender

In the present study, gender ration was disproportionate (411 female patients versus 50 male patients [89.2% vs. 10.8%]) and post-operative and transient hypocalcaemia was significantly more common in the female patients in both univariate ( $p=0.011$ ) and multivariate statistical analysis ( $p=0.047$ ) similar to the literature [72;69;73]. However, in rare cases, some studies reported conflicting results with respect to female gender as a risk factor for post thyroidectomy hypocalcaemia [74]. In our study we did not control for possible confounding factors which could in part explain our results as the female gender has various factors that can interact with calcium level. Women are more likely to have disease associated with a variety of hormones, such as menopausal syndrome, osteoporosis and vitamin D deficiency. Thus, evaluations of bone mineral density, menstruation status, and other hormones levels may be necessary [76;77]. However, preoperative vitamin D and preoperative bone mineral density were not measured in our study.

Furthermore as demonstrated in previous studies, there is a lower vitamin D level in women [75]. It is believed that preoperative vitamin D level can predict post thyroidectomy hypocalcaemia [76]. A Moroccan study by Allali F [77] on 415 women aged 24 to 77 years demonstrated that vitamin D deficiency (VDD) affects more than 90% of Moroccan women. In Morocco, vitamin D deficiency is linked to a lifestyle not favoring sun exposure particularly in relation to clothes covering the whole body and lack of activities outdoors limiting their exposition to sun. A retrospective study of 152 patients who underwent thyroidectomy in which patients with or without VDD were compared suggest that despite vitamin D deficiency being common in patients undergoing thyroidectomy, it doesn't increase the rate of hypocalcaemia. As a result, preoperative evaluation and repletion of vitamin D is unlikely to reduce post thyroidectomy hypocalcaemia rates [78].

On another note the observed gender difference can partially be accounted for at the molecular level by various regulators of monoclonal proliferation and mitosis of parathyroid tissue. Despite being characterized by a low rate of cell turnover and division, [79] mitosis of parathyroid cells can be stimulated by conditions of functional demand such as a hypocalcemic state [80]. Even if the precise molecular mechanisms involved in this process have yet to be defined, various growth factors and cell-cycle regulators have been implied [81]. Males may possess polymorphisms of these regulatory genes that confer them a proliferation advantage over females and that enhance their ability to maintain calcium homeostasis in conditions of transient functional demand.

The female predisposition to post thyroidectomy hypocalcaemia may also be iatrogenic in nature. Previous studies have shown the intensity and frequency of early hypocalcaemia to be directly related to the number of parathyroid glands preserved during surgery [82]. As found in a retrospective case series study with chart review of 270 consecutive total thyroidectomy patients, women had a slightly higher rate of accidental parathyroid gland removal. Perhaps, a greater degree of mechanical trauma is imposed upon the parathyroid glands of females during thyroidectomy because of a more diminutive operative field (meaning a smaller neck). Conceivably women are predisposed to a higher rate of accidental parathyroid gland removal during thyroidectomy. However, the clinical relevance of these findings is uncertain based on a modest sample size [83].

This implies that females could conceivably benefit from earlier and possibly preoperative calcium supplementation to help reduce its occurrence. As we found in a recent cohort study; preoperative calcium and calcitriol supplementation, in addition to routine postoperative supplementation, was associated with a decreased incidence of both biochemical and clinical hypocalcaemia, need for intravenous calcium repletion, and hospital readmissions [84].

#### ❖ **Preoperative hyperthyroidism:**

In our study population, preoperative hyperthyroidism was associated significantly with transient hypocalcaemia in the univariate analysis ( $p=0.029$ ) but not on the multivariate analysis ( $p=0.807$ ). Thus Transient hypocalcaemia was observed in 57 patients (39.9%) who had preoperative hyperthyroidism *versus* 92 patients (29.5%) with normal TSH level, with  $p=0.029$ . This result is

in correlation with the literature that found the incidence of transient hypocalcaemia seems to be higher for thyrotoxic patients compared with euthyroid patients undergoing thyroidectomy for other nontoxic benign thyroid nodules [85]. In addition a diagnosis of hyperthyroidism is independently associated with a difficult thyroidectomy [7;86] this may be due to hypervascularization of the thyroid gland during hyperthyroidism. In patients with hyperthyroidism, the postoperative reversal of osteodystrophy and the accretion of calcium in bones may contribute to the decreased serum calcium. However Hungry bone syndrome (HBS) has been postulated as a potential cause of postoperative hypocalcaemia in thyrotoxic subjects undergoing Thyroidectomy [87]. HBS is a well-established phenomenon after surgical management of primary hyperparathyroidism relating to the sudden decline in parathormone (PTH) levels postoperatively and consequent rapid skeletal uptake of calcium [88;89]. Furthermore prior reports [90] showed that HBS is likely to develop in thyrotoxic patients after thyroidectomy when there is severe depletion of BMD (bone mineral density) dependent on the severity and duration of the disease, rapid preparation for surgery with antithyroid drugs when bone formation is maximal, and injury or devascularization of parathyroid glands precipitating PTH fall .

On another note other studies suggest that the risk of hypocalcaemia is not alleviated by the correction of hyperthyroidism within a few weeks before thyroidectomy [91]. It is correlated with the pretreatment serum levels of free thyroxine [92] and with markers of the bone turnover rate, such as serum alkaline phosphatase levels [93] and urinary hydroxyproline [88]. Euthyroidism before surgery and more importantly a prolonged period of euthyroidism before surgery may prevent the occurrence of post-operative hypocalcaemia for patients with hyperthyroidism.

### ❖ **Preoperative hypocalcaemia:**

As expected, our study demonstrated that preoperative hypocalcaemia is significantly correlated with post-operative hypocalcaemia and transient hypocalcaemia on both univariate ( $p=0.001$ ) and multivariate ( $p=0.001$ ) analysis, while it wasn't significant when it came to permanent hypocalcaemia. The same results were found in prior retrospective study of 349 patients undergoing thyroidectomy [94].

It is established that Calcium absorption is regulated primarily via parathyroid hormone and vitamin D. In our study we were not able to assess the effect of preoperative vitamin D because none of our patients had their vitamin D level measured preoperatively. Vitamin D3 (cholecalciferol) is acquired via diet or photon-stimulated conversion of precursors in the skin. In the liver, it is hydroxylated to 25- hydroxyvitamin D3 (calcifediol), which, due to its half-life of 2 to 3 weeks, is the most useful measure of vitamin D levels. When stimulated by parathyroid hormone, the enzyme  $1\alpha$ - hydroxylase in the kidney further hydroxylates 25-OHD3 to the active form 1,25-dihydroxyvitamin D3 (calcitriol). Activated vitamin D increases calcium absorption from the intestine. Thus Vitamin D deficiency is a known independent risk factor for post-thyroidectomy hypocalcaemia. Secondary hyperparathyroidism due to low calcium and vitamin D levels is thought to be the mechanism behind the increased risk of hypocalcaemia in patients with vitamin D deficiency [95;96].

### ❖ **Type of Intervention :**

In this case series, our patients were divided into 2 groups according to the type of intervention; group 1 includes patients undergoing unilateral intervention and group 2 includes patients undergoing bilateral intervention. We found the rate of post-operative and transient hypocalcaemia significantly higher among the 2nd group of patients undergoing bilateral interventions ( $p < 0.001$ ). This may seem to be an obvious result as during unilateral intervention, only one side is explored, thus only exposing 2 parathyroid glands while the contralateral remnant lobe remains intact. It is known that a single functioning gland is able to maintain calcium metabolism at normal values [97].

### ❖ **Extent of surgery :**

In this study central neck dissection and lateral neck dissection (LND) were found to be of no significance ( $p = 0.829$ ) whereas the extent of the central neck dissection (CND) was significant in the development of post thyroidectomy hypocalcaemia ( $p = 0.038$ ). Thus, patients who got bilateral dissection had an increased rate of post-operative and transient hypocalcaemia than patients who got unilateral dissection. Considering the general anatomical location of the PTGs it is less likely that LND will affect the development of hypoparathyroidism.

In a retrospective study on 1030 patients who had undergone total thyroidectomy, they found CND not to be significant on multivariate analysis but the extent of CND was significant similarly to our findings [98]. They suggest that this may mean that the CND itself was more likely to have damaged the PTG, because the preserved contralateral PTG in patients who underwent unilateral CND in whom the ipsilateral PTG was sacrificed might have prevented the development of hypoparathyroidism. Although one study found no correlation between CND and hypocalcemia [2], and the technique of CND may be the important factor in preserving the PTG [99], if one considers the general anatomical location of these glands (especially the lower PTG), CND can potentially injure them.

#### ❖ **Inadvertent PTG and auto implantation of PTG:**

For seemingly obvious reasons in the present study, inadvertent parathyroidectomy was a significant factor in initial and transient post thyroidectomy hypocalcaemia ( $p=0.018$ ). In a retrospective cohort study [100] which included 2556 patients who underwent total thyroidectomy they found that the number of incidentally resected PTGs is strongly associated to the risk of temporary and permanent hypocalcaemia, thus there was a significant higher risk of temporary and permanent hypocalcaemia in patients who had two parathyroid glands resected compared to those who had only one gland incidentally resected. Moreover, patients who had three incidentally resected parathyroid glands showed a significantly higher incidence of permanent hypocalcaemia compared to those patients with 2 incidentally resected parathyroid glands. However a prospective study on 200 patients who underwent thyroidectomy found no significant correlation between incidental

parathyroidectomy and clinical and biochemical postoperative hypocalcaemia ( in the study after resection, the thyroid gland surface was carefully examined for the presence of parathyroid tissue and the parathyroid glands were auto transplanted using a standard technique) [101].

On another note, except for 1 PTG (that was intracapsular so its removal was unavoidable) that was considered unviable all 35 PTGs that were accidentally removed were transplanted in the SCM. So analyzing inadvertent parathyroidectomy and auto implantation in relations to post-operative hypocalcaemia results in the same interpretation. In our study we found that auto transplantation was significantly relevant in post-operative ( $p=0.028$ ) and transient hypocalcaemia ( $p=0.014$ ). We are not able to evaluate the efficiency of auto-transplantation of PTGs as an independent variable. In addition, this suggests that auto transplantation of PTGs after accidental resection is of no value in decreasing the incidence of post thyroidectomy hypocalcaemia. In agreement to our results, a recent prospective study [102] found that the prevalence of parathyroid failure syndromes after total thyroidectomy was similar whether a parathyroid gland was inadvertently excised or auto transplanted and that auto transplantation did not influence the permanent hypoparathyroidism rate. A more recent narrative review by the same team [103] found the absence of proof of clinically significant PTG graft function. They reported that it remains hard to prove that auto transplanted normal parathyroid tissue takes well into a muscle or subcutaneous pocket and that is functional and able to reduce the permanent hypoparathyroidism rates. The presence of other potentially functioning glands remaining in situ after thyroidectomy and the absence of a clear cut proof of function due to

impossibility of venous sampling close to the sternocleidomastoid muscle have obscured the benefits of PAT and have been a serious theoretical obstacle for those claiming a benefit thyroidectomy. Both studies recommend that both parathyroid auto transplantation and inadvertent parathyroidectomy should be avoided and all efforts should be made to preserve the parathyroid glands in situ.

#### ❖ **PTGs Identification :**

In our study, identification of PTGs was not significantly associated with a lower incidence of transient or permanent hypocalcaemia ( $p=0.649$  for bilateral intervention and  $p=0.375$  for unilateral intervention). Nevertheless, patients undergoing bilateral intervention who had less than 2 PTGs identified during surgery had lower incidence of post thyroidectomy transient hypocalcaemia than those who had more than 2 PTGs seen during intervention (31.3% *versus* 36.3%). This is in correlation with a study done on 569 patients found that when the extra-capsular technique was adopted during total thyroidectomy, identifying fewer PGs in their orthotopic positions not only lowered risk of temporary and protracted hypoparathyroidism but also shortened recovery from protracted hypoparathyroidism [104]. Some authors suggest that this is due to the risk of injury inherent to parathyroid manipulation [105]. However there is no consensus on the recommendation to identify the PTGs in order to preserve them or on the minimum number of glands to be preserved [106]. In a retrospective study done 254 patients, the authors suggest that a careful dissection of the thyroid capsule as close as possible to the thyroid parenchyma as well as the identification of the PTGs prior to ligation of the inferior thyroid artery are important both to avoid damaging the structure and vascularization, and to prevent accidental removal along with the thyroid lobe [107].

### ❖ Age :

In this study, we did not find significant difference in the mean age between patients who developed post-operative hypocalcaemia and those who didn't (48.7 +/- 13.7 *versus* 47.7 +/- 14.6 years,  $p= 0.477$ ). It is the same observation when it comes to transient hypocalcaemia (49.2 +/- 13.7 years *versus* 47.5 +/- 14.5 years,  $p=0.234$ ) and permanent hypocalcaemia (39.6 +/- 9.8 years *versus* 48.2 +/- 14.3 years,  $p= 0.092$ ). This could be explained by the fact that in our study the mean age of the population (48 +/- 14.3 years old) is a lot younger than in the literature [107;108]. However, there are studies similarly to ours that have noted limited association between older age and outcome due to thyroidectomy. A prospective study [109] done on a population of 85 patients and 44 thyroidectomy patients aged 21 to 35 years versus  $\geq 65$  years respectively , showed no difference in complication rates between younger and older patients.

The influence of age on post thyroidectomy hypocalcaemia still needs to be clarified in view of other confounding patient and disease related factors. A retrospective cohort study using the American college of surgeons national surgical quality improvement program database found that a higher rate of post thyroidectomy complications in patients aged 65 to 79 years. They also found a higher rate of complications, higher rates of overall and related readmission with extended length of hospital stay in patients aged  $\geq 80$  years [110]. Older age is associated with vitamin D deficiency [111] , probably due to reduced skin 7-dihydrocholesterol, decreased renal 1  $\alpha$ -hydroxylase activity and reduced calcium absorption [112].

### ❖ Previous thyroid intervention :

Contrary to some studies that conclude that completion thyroidectomy can increase post-operative complications such as hypoparathyroidism [113]. In our study we found an increase in the incidence of post-operative, transient and permanent hypocalcaemia among patients undergoing thyroidectomy for the 1st time, however it was not statically significant ( $p=0.108$ ). Similarly to our results, a retrospective study performed at the McGill University Thyroid Cancer Center, Montreal, Quebec, Canada, reported that the occurrence of transient hypocalcaemia was significantly lower in the completion thyroidectomy (CT) patient group than in the total thyroidectomy (TT) patient group. And that transient hypocalcaemia occurred in 1.5% of patients after CT and 12.5% after TT but there was no significant difference in the occurrence of permanent hypocalcaemia between the two groups [114].

In case of completion thyroidectomy, the devitalized parathyroid can be revascularized before the second surgical intervention because of the time interval between the completion thyroidectomy and the 1st operation. This can result in a decreased rate of post thyroidectomy hypocalcaemia [115].

A few researches suggest that completion thyroidectomy can increase postoperative complications such as hypoparathyroidism, especially when they are performed by inexperienced surgeons [108]. It is known that surgeons with sufficient experience can perform iterative thyroidectomy with low morbidity [116]. The difficulty in completion thyroidectomy comes from the post-operative fibrosis thus increased risk of PTGs injury [117]. They recommend that completion thyroidectomy should be performed within 10 days or at least 3 months after the first surgery to avoid postoperative fibrosis in the operative field [118;119].

## ❖ **Diagnosis :**

### **- Thyroid cancer :**

In our study we found that the diagnosis of thyroid cancer was not related to post-operative hypocalcaemia. The incidence of post thyroidectomy was higher in patients with other diagnosis (37.5%) than patients with thyroid cancer (31.5%). It correlates with the results of a retrospective results study by Stravos Gourgiotis et al [120] who found that the incidence of inadvertent parathyroidectomy was inversely correlated with thyroid malignancy ( $p < 0.005$ ). Thus suggesting that thyroid malignancy may reduce the incidence of inadvertent parathyroidectomy. It may be explained by the fact that in their study population there was no patient with advanced thyroid malignancy and there was no case with extensive thyroid procedure and perhaps the surgical techniques may be more meticulous in cases with suspected malignancy.

However malignant neoplasm are commonly considered to be risk factors for post thyroidectomy hypocalcemia in multiple studies [121;122; 117]. Some authors believe that malignancy tends to be treated with a more aggressive approach to thyroid surgery, thereby leading to incidental parathyroidectomy and hypocalcemia [131]. The altered anatomy of these patients could increase the likelihood of parathyroid tissue removal.

### **- Graves disease:**

Though it wasn't significant, we found that patients with Graves disease (GD) had a higher incidence of post-operative and transient hypocalcaemia than patients with thyroid cancer and MNG (38.5% versus 35.7%, with  $p = 0.842$ ). Multiple studies including a study conducted in our department on a different set

of patients then ours that compared Graves disease *versus* MNG [61] reported that Graves disease is a well known risk factor for post-operative hypocalcaemia [123 ;124]. This may be due to the influence of thyroid hormones on calcium metabolism and bones, as they accelerate bone formation and remodeling [125]. A decrease in thyroid hormones results in an alteration of the calcium balance, leading to “hungry bone” syndrome which is manifested through hypocalcaemia, hypophosphatemia and hypomagnesaemia [126]. In these patients with hyperthyroidism, anti-thyroid treatment usually improves the bone involvement caused by Graves disease [118].

In addition the fact that there is a greater vascularization with increased hemorrhage risk and the existence of a severe adherence of the thyroid capsule with the PTGs in Graves disease is an added difficulty for the identification and preservation of the parathyroid glands [100;127;1].

#### ❖ HTA and Diabetes

When it comes to the relation between the occurrence of post-operative, transient, permanent hypocalcaemia and hypertension we didn't find a significant difference ( $p=0.253$ ). We did not find information in regards to the relation between hypertension and post thyroidectomy hypocalcaemia in the literature. However, a retrospective study with a sample of 2559 patients found that hypertension is in relation with the occurrence of another thyroidectomy complication; postoperative hematomas. Thus their study found that 16 out of 32 patients (50%) who underwent surgical revision had hypertension; incidence of hematoma was 2.09% in patients with hypertension and 0.89% in patients without it ( $p<0.05$ ) [128]. In our study none of the patients who developed hematomas or hemorrhage had hypertension.

The same result was observed when it comes to diabetes; there was no significant difference between diabetic patients and non diabetic patients when it come to the occurrence of post-operative ( $p=0.737$ ), transient ( $p=0.919$ ) and permanent hypocalcaemia ( $p=1.000$ ). We did not find information in regards to the relation between diabetes and post thyroidectomy hypocalcaemia.

#### ❖ **Thyroid size :**

Thyroid size was assessed on ultrasound, and we found that large thyroid volume was not significantly related with post-operative hypocalcaemia ( $p=0.261$ ). Patients with large thyroid volume had lower incidences in rates of post-operative hypocalcaemia. However In the literature we found that large thyroid size (maximum thyroid diameter  $> 50\text{mm}$ ) and volume (volume  $> 25\text{ml}$ ) was related with an increased risk of incidental parathyroidectomy [109], this may be explained by technical difficulty during surgery and the frequent association between large thyroid gland and hypervascularization of the gland.

#### ❖ **Surgical expertise :**

In our study we found that there was no significant differences when it comes to post-operative hypocalcemia between interventions done by senior surgeons and residents ( $p=0.190$ ). Although it wasn't significant we found that post thyroidectomy hypocalcemia was observed more with surgeries performed by senior surgeons (33.1% *versus* 21.9%). This may be due to the fact that senior surgeons tend to focus less on surgical precision after long years of performing numerous thyroidectomies.

In the literature the surgeon's experience is relevant to avoid post thyroidectomy complications in general. A prospective cross sectional multicenter study found that patients were at increased risk of permanent complications after thyroidectomy performed by less experienced surgeons and by those in practice for 20 years or more, suggesting that surgeons aged 35 to 50 years provided the safest care [129].

## II-POST OPERATIVE DYSPHONIA:

Thyroidectomy may result in vocal impairment due to extrinsic compression of the gland on the larynx, endotracheal intubation, dissection of the cervical muscles, hematomas, and damage to the laryngeal nerves. Dysphonia may occur in up to 90% of patients, especially in the immediate postoperative period and persist for three to 6 months in 11-15% of cases [130]. The recurrent laryngeal nerve (RLN) as well as the external branch of the superior laryngeal nerve (SLN) can be temporarily or permanently injured. The estimated rates of injury to the SLN vary from 0.3% to 13% and to the RLN from 5% to 10%, being temporary in 5% and permanent in 0.5 -2% [131]. Damage to the RLN is the main cause of dysphonia after thyroidectomy [132 - 133].

In this study, suspected lesion of RLN during intervention was the only significant factor in the development of post thyroidectomy dysphonia in univariate analysis ( $p=0.026$ ) however it wasn't relevant on multivariate analysis. In addition suspected lesion of the recurrent nerve was not significantly related to post thyroidectomy hypocalcaemia ( $p=0.343$ ), however the incidence of post thyroidectomy hypocalcaemia was higher in patients with patients suspected lesion of the RLN than patients without lesion of the RLN (60% *versus* 33.8%).

On another note in our series out of the 5 patients who had suspected lesion of the RLN during surgery only 1 patient (2.8%) sustained inadvertent Para thyroidectomy ( $p= 0.335$ ). In contradiction to our results a retrospective cohort study which included 2556 patients who underwent total thyroidectomy found

that the incidence of IP was 7 fold higher in patients with RLN injury compared with the no-RLN injury group [101]. Eventually, the anatomical variations of the RLN (especially the right) and the different locations of the parathyroid glands may play a role. The proximity of parathyroid glands to the RLN, makes them more vulnerable to devascularization or resection in cases of RLN injury.

The reported risk factors of laryngeal nerve damage in thyroidectomy are: goiter greater than 5 cm, patients older than 50 years, reoperation, malignant disease, type of surgery (partial or total thyroidectomy, with or without lymph node dissection), and surgeon experience [134;135]. Other causes include perineural vascular injury and compression by hematoma.



In this retrospective study of thyroidectomy performed at the surgical department “A” at Ibn Sina over a 12 years period, we were able to identify patient related clinical and surgical risk factors for post thyroidectomy hypocalcaemia. Thus, we found female gender, preoperative hypocalcaemia, and bilateral intervention to be independent predictors of post-operative and transient hypocalcaemia. Additionally, in patients with preoperative hyperthyroidism, bilateral CND, 1<sup>st</sup> time thyroidectomy, and inadvertent thyroidectomy confers an increased risk of developing transient hypocalcaemia .We also confirmed that suspected lesion of the RLN is a risk factor for post-operative dysphonia. Based on our experience preoperative hypocalcaemia dosage should be systematic for all patients undergoing thyroidectomy and preoperative vitamin D evaluation for women should be considered. Perhaps preoperative calcium treatment and vitamin D supplementation for patients with risk factors may prevent post thyroidectomy hypocalcaemia, a prospective study need to be done to convey on the efficiency.



# ABSTRACT

**Title:** Incidence and predictive factors of post thyroidectomy hypocalcaemia

**Key Words:** Thyroidectomy, Hypocalcaemia, Post-thyroidectomy complications, Dysphonia

**Author:** HABTE Eden Ayele

## **Background:**

Hypocalcaemia is a frequent complication of thyroidectomy. Although typically transient, it can lead to an increased length of hospitalization, readmission, and in rare cases be permanent with a lifetime supplementation of calcium.

## **Objective:**

The aim of this study was to determine the incidence of hypocalcaemia in patients undergoing different type of thyroidectomy for different pathologies, in order to determine which are the factors that could be used as predictive indicators of post-operative, transient and permanent hypocalcaemia.

## **Materials and Methods:**

This retrospective study consisted of 461 patients who had undergone thyroidectomy at the surgical department “A” in IbnSina Hospital between January 2007 to December 2018. The clinicopathologic, biological and surgical details of normocalcemic and hypocalcemic patients were compared.

## **Results:**

Out of the 461 patients 157 patients (34.1%) developed initial post-operative hypocalcaemia, 149 of them (32.3%) were found to have transient hypocalcaemia and 8 of them (1.7%) had permanent hypocalcaemia.

Univariate analysis found female gender ( $p=0.009$ ), preoperative hypocalcaemia ( $p=0.001$ ), preoperative hyperthyroidism (0.029), bilateral intervention ( $p=0.000$ ), bilateral central neck dissection ( $p=0.038$ ) and inadvertent parathyroidectomy ( $p=0.018$ ) to be significantly associated with transient hypocalcaemia.

Multivariate analysis demonstrated that female gender ( $p=0.047$  OR: 2.87), preoperative hypocalcaemia ( $p=0.001$  OR: 22.21) and bilateral intervention ( $p=0.002$  OR: 15.66) were independent significant factors.

In addition suspected lesion of the RLN during surgery was a significant factor for post-operative dysphonia on univariate analysis.

## **Conclusion:**

In conclusion female gender, preoperative hypocalcaemia and bilateral intervention increase the risk of developing transient hypocalcaemia. Preoperative evaluation of calcemia should be systematic and preoperative management of hypocalcaemia should be initiated in patients that are at high risk of developing hypocalcaemia after thyroidectomy.

# RÉSUMÉ

**Titre :** Incidence et facteurs prédictifs de l'hypocalcémie en post thyroïdectomie

**Mots clés :** Thyroïdectomie, hypocalcémie, complication post thyroïdectomie, Dysphonie

**Auteur :** HABTE Eden Ayele

## **Introduction et Objective:**

L'hypocalcémie est une complication fréquente de la thyroïdectomie. Bien qu'elle soit généralement transitoire, dans des cas rares elle peut être permanente. Le but de cette étude est de détecter l'incidence de l'hypocalcémie chez les patients subissant différents types de thyroïdectomie pour certaines pathologies thyroïdiennes, pour déterminer les facteurs qui pourraient servir d'indicateurs prédictifs d'une hypocalcémie postopératoire, transitoire et permanente.

## **Patients et méthodes:**

Cette étude rétrospective comprend 461 patients ayant subi une thyroïdectomie au service de chirurgie « A » de l'hôpital Ibn Sina entre janvier 2007 et décembre 2018. Les détails clinicopathologiques, biologiques et chirurgicaux des patients normocalcémiques et hypocalcémiques ont été comparés.

## **Resultats :**

Sur les 461 cas, 157 patients (34,1%) ont développé une hypocalcémie postopératoire, dont 149 (32,3%) une hypocalcémie transitoire, pour les 8 patients restants (1,7%) il s'agit d'une hypocalcémie permanente.

L'analyse univariée a démontré que le sexe féminin ( $p = 0,009$ ), l'hypocalcémie préopératoire ( $p = 0,001$ ), l'hyperthyroïdie préopératoire ( $p = 0,029$ ), l'intervention bilatérale ( $p = <0,001$ ), la dissection centrale bilatérale du cou ( $p = 0,038$ ) et la parathyroïdectomie accidentelle ( $p = 0,018$ ) sont associées de manière significative à l'hypocalcémie transitoire.

Quant à l'analyse multivariée, elle a démontré que le sexe féminin ( $p = 0,047$  OR: 2,87), l'hypocalcémie préopératoire ( $p = 0,001$  OR : 22,21) et l'intervention bilatérale ( $p = 0,002$  OR: 15,66) sont des facteurs significatifs indépendantes.

## **Conclusion :**

Donc le sexe féminin, l'hypocalcémie préopératoire et l'intervention bilatérale augmentent le risque de développer une hypocalcémie transitoire. L'évaluation préopératoire de la calcémie doit être systématique et une prise en charge préopératoire de l'hypocalcémie doit être initiée chez les patients à haut risque de développer une hypocalcémie après thyroïdectomie.

## ملخص

**العنوان :** الإصابة والعوامل التنبؤية لنقص كلس الدم بعداستئصال الغدة الدرقية.

**الكلمات المفتاحية:** استئصال الغدة الدرقية،نقص كلس الدم ،المضاعفات بعدا ستئصال الغدة الدرقية،بحة الصوت.

**الكاتبة :** هابتايدنايل.

### المقدمة والهدف:

نقص الكالسيوم في الدم هو أحد المضاعفات الشائعة لاستئصال الغدة الدرقية .  
الهدف من هذه الدراسة هو تحديد حالات نقص الكالسيوم في الدم في المرضى الذين يخضعون لإستئصال الغدة الدرقية لأسباب مرضية مختلفة ،  
من أجل تحديد العوامل التي يمكن استخدامها كمؤشرات تنبؤية من نقص كلس الدم العابر او الدائم بعد العملية الجراحية.

### المرضى والطرق:

تشمل هذه الدراسة بأثر رجعي 461 مريضاً خضعوا لاستئصال الغدة الدرقية في قسم الجراحة أ بمستشفى ابن سينا بين يناير 2007 الى ديسمبر 2018.  
وتمت مقارنة التفاصيل الإكلينيكية والبيولوجية والجراحية للمرضى الذين يعانون من نقص كلس الدم والذين لا يعانون منه.

### النتائج :

من بين 461 مريض ، أصيب 157مريضاً (34.1) ٪ (بنقص كلس الدم بعد العملية الجراحية ، 149 منهم32.3) ٪ (كانوا يعانون من نقص كلس الدم العابر و 8 منهم 1.7) ٪ (من نقص كلس الدم الدائم.  
في التحليل أحادي المتغير ، الجنس الأنثوي ( $p = 0.009$ ) ، نقص كلس الدم قبل الجراحة ( $p = 0.001$ ) ، فرط نشاط الغدة الدرقية قبل الجراحة (0.029) ، الجراحة الثنائية ( $p = <0.001$ ) ، التشريح المركزي الثنائي للعنق ( $p = 0.038$ ) واستئصال جارات الدرق العرضي ( $p = 0.018$ ) مرتبطة بشكل كبير مع نقص كلس الدم العابر .  
في التحليل متعدد المتغيرات ، كان جنس الإناث ( $p = 0.047$  OR 2.87) ، ونقص كلس الدم قبل الجراحة ( $p=0.001$  OR 22.21) والجراحة الثنائية ( $p = 0.002$  OR 15.66) عوامل مهمة .

### الخلاصة:

الجنس الأنثوي ، نقص كلس الدم قبل الجراحة والجراحة الثنائي تزيد من خطر الإصابة بنقص كلس الدم العابر .  
يجب أن يكون تقييم ما قبل الجراحة لكلس الدمهجيأ ويكون العلاج ما قبل الجراحة لنقص كلس الدم في المرضى المعرضين لخطر كبير بتطور نقص كلس الدم بعد استئصال الدرقية.



**Data collection for the research of incidence of hypocalcaemia for patients undergoing thyroidectomy**

F     M

Name/Surname: \_\_\_\_\_ Age: \_\_\_\_\_ Originally from: \_\_\_\_\_ Profession: \_\_\_\_\_  
 Consultation Date: \_\_\_\_\_ Date of Surgery: \_\_\_\_\_ Hospital discharge date: \_\_\_\_\_

**THYROID PATHOLOGY :** Graves disease  Large Goiter  Thyroid Cancer  Solitary Nodule  HMN

**Health Backgrounds: Personal** \_\_\_\_\_

**Family history** \_\_\_\_\_

**Clinical findings:**

Symptoms present since \_\_\_\_\_ Pain    Compression signs    Hyperthyroidism signs    Hyperparathyroidism signs  
 Hypothyroidism signs    ORL examination: Vocal cords ; intact pathological ; \_\_\_\_\_

**Medical Imagery:**

**Ultrasound :** \_\_\_\_\_ Lymph Nodes: L R

**CT scan:** not done    Done ; \_\_\_\_\_

**Scintigraphy ;** Not done    Done ; \_\_\_\_\_

**Chest X-ray:** Calcifications    signs of compression/deviation    Plunging Goiter

**Laboratory Profile:** TSH = \_\_\_\_\_ T<sub>3</sub> = \_\_\_\_\_ T<sub>4</sub> = \_\_\_\_\_  
 Ca<sub>2+</sub> = \_\_\_\_\_ P = \_\_\_\_\_ PTH = \_\_\_\_\_

Renal function: N  A  \_\_\_\_\_ Liver function : N  A  ;

Thyroglobulin = \_\_\_\_\_ Calcitonin level = \_\_\_\_\_

**Fine Needle Aspiration Biopsy :** not done    done ; \_\_\_\_\_

**Preoperative medication:** \_\_\_\_\_

**Surgical indication :** Recurrent hyperthyroidism after medical treatment  mechanical obstruction by large goiter   
 Suspicious nodule in fine needle aspiration  complaints of discomfort with medical treatment   
 Ophthalmopathy in young patient  Patients choice of treatment   
 Other; \_\_\_\_\_

**Type of surgery:** TT/NTT    STT    L/HT     left  right    IT    **Duration of surgery:** \_\_\_\_\_

**Surgical approach** Cervicotomy alone  associated Sternotomy

**Surgical Techniques and Incidents:**

**RLN:** Detection of the RLN \_\_\_\_\_ lesion  section  Sacrificed

**PGs:** detection of PGs \_\_\_\_\_ parathyroid incidentaloma

Incidental parathyroidectomy    Sacrificed    Autotransplantation \_\_\_\_\_

**Extent of surgery:** \_\_\_\_\_

**Injury of other organs:** No  Yes  \_\_\_\_\_

**Anatomical Pathology Specimen:** Size = \_\_\_\_\_

Identification of PGs in specimen No  Yes  ; number: \_\_\_\_\_ location: \_\_\_\_\_

Histopathology: \_\_\_\_\_

Extent of invasion if present: Capsular  vascular  lymph node metastases

**Postoperatively: Day 1 - Day 2**

Symptoms of hypocalcaemia    Dysphonia    Hematomas    Operative wound infection    Hemorrhage

Laboratory profile: Ca<sub>2+</sub> :D1= \_\_\_\_\_ D2 = \_\_\_\_\_ P :D1= \_\_\_\_\_ D2= \_\_\_\_\_ PTH= \_\_\_\_\_

Supplementation: No  Yes  \_\_\_\_\_

**Long Term Check Up :** Date \_\_\_\_\_ Symptoms of hypocalcaemia;    Dysphonia

Phosphorus = \_\_\_\_\_ Calcemia    \_\_\_\_\_ PTH= \_\_\_\_\_ TSH= \_\_\_\_\_

Supplementation \_\_\_\_\_

**Surgeons :** Senior surgeon  Residents

**Annex 1: Data collection form.**



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## *Serment d'Hippocrate*

*Au moment d'être admis à devenir membre de la profession médicale, je m'engage solennellement à consacrer ma vie au service de l'humanité.*

- *Je traiterai mes maîtres avec le respect et la reconnaissance qui leur sont dus.*
- *Je pratiquerai ma profession avec conscience et dignité, la santé de mes malades sera mon premier but.*
- *Je ne trahirai pas les secrets qui me seront confiés.*
- *Je maintiendrai par tous les moyens en mon pouvoir l'honneur et les nobles traditions de la profession médicale.*
- *Les médecins seront mes frères.*
- *Aucune considération de religion, de nationalité, de race, aucune considération politique et sociale ne s'interposera entre mon devoir et mon patient.*
- *Je maintiendrai le respect de la vie humaine dès la conception.*
- *Même sous la menace, je n'userai pas de mes connaissances médicales d'une façon contraire aux lois de l'humanité.*
- *Je m'y engage librement et sur mon honneur.*

## قسم أبقراط

بسم الله الرحمن الرحيم

أقسم بالله العظيم

في هذه اللحظة التي يتم فيها قبولي عضوا في المهنة الطبية أتعهد علانية :

- < بأن أكرس حياتي لخدمة الإنسانية .
- < وأن أحترم أساتذتي وأعترف لهم بالجهد الذي يستحقونه .
- < وأن أمارس مهنتي بواجب من ضميري وشرعية في جاعة لاصحة مرضي هدي في الأول .
- < وأن لا أفشي الأسرار المعهودة إلي .
- < وأن أحافظ بكل ما لدي من وسائل على الشرف والتقاليد النبيلة لمهنة الطب .
- < وأن أعتبر سائر الأطباء إخوة لي .
- < وأن أقوم بواجبي نحو مرضاي بدون أي اعتبار ديني أو وطني أو عرقي أو سياسي أو اجتماعي .
- < وأن أحافظ بكل حزم على احترام الحياة الإنسانية منذ نشأتها .
- < وأن لا أستعمل معلوماتي الطبية بطرق يضر بحقوق الإنسان مهما لاقيت من تهديد .
- < بكل هذا أتعهد عن كامل اختياري ومقسما بالله .

والله على ما أقول شهيد .



المملكة المغربية  
جامعة محمد الخامس بالرباط  
كلية الطب والصيدلة  
الرباط



جامعة محمد الخامس بالرباط  
Université Mohammed V de Rabat

أطروحة رقم: 107

سنة : 2020

## الإصابة والعوامل التنبؤية لنقص كلس الدم بعد استئصال الغدة الدرقية

### أطروحة

قدمت ونوقشت علانية يوم : / / 2020

### من طرف

السيدة ايدين ايلي هابت  
المزادة في 09 نونبر 1994 بأديس أبابا (إثيوبيا)

### لنيل شهادة

### دكتور في الطب

**الكلمات الأساسية :** استئصال الغدة الدرقية؛ نقص كلس الدم؛ المضاعفات بعد استئصال  
الغدة الدرقية؛ بحة الصوت

### أعضاء لجنة التحكيم:

رئيس	السيد لحسن إفرين أستاذ في الجراحة العامة
مشرف	السيد الحاج عمر المالقي أستاذ في الجراحة العامة
عضو	السيدة هند العراقي أستاذة في أمراض الغدد وأمراض الأيض
عضو	السيد المنتصر الشريف الشفشاوني أستاذ في الجراحة العامة