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Risk of Hypocalcemia After Total Thyroidectomy and Bilateral Central Neck Dissection in Patients With Papillary Thyroid Carcinoma

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Abstract

Background: One of the most common adverse effects after thyroid surgery is hypocalcemia, which can result in symptoms ranging from paresthesia to laryngospasm. We can prevent the requirement for calcium and vitamin D pills for the rest of our lives if we can avoid this problem.

Aim: Evaluation of hypocalcemia following bilateral central neck dissection for papillary thyroid cancer and complete thyroidectomy, as well as strategies to prevent it.

Patients and methods: This study involved 30 patients with papillary thyroid carcinoma who were admitted to Sayed Galal Hospital. The patients' serum calcium and parathormone levels were assessed to screen for postoperative hypocalcaemia after a complete thyroidectomy and central neck dissection. They were then split into three groups: B, C, and A.

Results: Patients in group B experienced temporary hypocalcemia and had normal parathyroid hormone levels, indicating parathyroid dysfunction. It took an average of 15.5 days for the calcium levels to return to normal range. Parathyroid hormone levels were below the normal range in group C patients, who had hypocalcemia for more than 6 months, indicating absolute hypoparathyroidism.

Patients in group C were older, less likely to be female, had somewhat larger tumors, and showed symptoms later in the disease progression in terms of age, gender, tumor size, and stage. Preoperative calcium levels were not linked to risk since group C patients had the highest mean of ionized calcium and group B patients had a lower mean of total calcium level than group C.

Conclusion: The primary risk factor for hypocalcemia following thyroidectomy is a surgical technique. Preserving the parathyroid themselves requires as much care and dissection as necessary to maintain the parathyroid tissue's and the glands' blood supply. Older age, big tumors, and late stages are additional risk factors.

Keywords: Central neck dissection, Hypocalcemia, Hypoparathyroidism, Papillary thyroid carcinoma, Total thyroidectomy

1. Introduction

Thyroid carcinoma ranks as the fifth most prevalent form of cancer among women in Egypt.¹

Numerous pathogenic variants exist, with the papillary variety being the most prevalent, accounting for around 85% of cases. The user's text is

too short to be rewritten academically. Papillary carcinoma exhibits numerous histopathologic subgroups.²

Malignant cells have the ability to spread through the lymphatic system. They are situated close to the vein drainage of the gland. The dissemination of this phenomenon is primarily directed towards the lymph nodes that drain situated in level VI of the neck.³

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The parathyroid glands, located close to the thyroid gland, have a vital function in regulating calcium homeostasis in the bloodstream by releasing parathyroid hormone (PTH).⁴

Surgical intervention is crucial in the therapeutic management of papillary thyroid carcinomas.⁵

The occurrence of postoperative hypocalcemia can arise as a potential problem following surgical procedures, and it can manifest as either a temporary or chronic condition.⁶

The clinical presentation of hypocalcemia encompasses a range of symptoms, which may include sensory numbness, tetany, and laryngeal spasm, among others.⁷

This occurrence occurs due to the trauma imposed upon the parathyroid glands or the constriction of their blood supply during surgical procedures.⁸

2. Patients and methods

The present investigation was carried out on a cohort of 30 individuals diagnosed with papillary thyroid cancer and cervical lymphadenopathy who were admitted to Sayed Galal University Hospital during the timeframe spanning from October 2022 to October 2023. The study involved the implementation of complete thyroidectomy and bilateral central neck dissection on patients, followed by a 6-month evaluation of hypocalcemia. The assessment was carried out by analyzing the concentrations of postpartum total and ionized calcium for all participants, and assessing the PTH level specifically in patients who experienced hypocalcemia.

In this study, informed consent was obtained from each patient before their inclusion. The informed consent involved providing a comprehensive explanation of the study as a research endeavor, as well as disclosing the specific details of the procedure, along with the expected benefits and any problems.

The diagnosis of patients was established by a comprehensive approach that included a detailed medical history, a thorough clinical examination, the use of neck ultrasonography, and, in more severe cases, neck computed tomography. Additionally, pathological evaluation through fine-needle aspiration cytology was employed to confirm the diagnosis further.

2.1. Exclusion criteria

The patient's medical history includes a prior neck surgery and a diagnosis of hypoparathyroidism. Additionally, the patient is now undergoing iodine therapy and has illnesses related to calcium metabolism, such as chronic renal disease and sarcoidosis.

A comprehensive examination of patients' detailed medical histories was conducted, encompassing factors such as age, gender, and medical and pharmaceutical backgrounds. Data about these variables was systematically gathered.

A comprehensive physical examination was conducted, which encompassed voice assessment and indirect laryngoscopy.

Preoperative laboratory analyses were conducted, encompassing assessments of free T3, free T4, and TSH, as well as serum total and ionized calcium levels. A neck ultrasound was performed on all patients, whereas computed tomography scans were reserved for individuals with advanced malignancies. A fine-needle aspiration cytology procedure was performed on all patients to obtain a pathological diagnosis. Only cases exhibiting well-differentiated carcinomas were included in the study.

The individuals involved in this research had an extracapsular complete thyroidectomy. The surgical procedure involved the removal of core nodes on both sides. Throughout the treatment, meticulous attention was devoted to preserving all parathyroid glands and their respective vascularization. The accomplishment involved the division of the branches of the inferior thyroid arteries responsible for supplying the thyroid gland while preserving the primary inferior thyroid arteries and their associated branches that nourish the parathyroid glands. The calcium levels, including total and ionized forms, were evaluated on the first day after the surgical intervention.

In hypocalcemia, the concentration of PTH was assessed and a more rigorous surveillance of serum calcium levels was implemented. Patients diagnosed with hypocalcemia were initiated on calcium and vitamin D supplementation while concurrently monitoring their serum calcium levels while the process of gradually reducing the dosage.

2.2. Follow-up

Follow-up appointments were arranged for all patients at intervals of 1, 2, and 6 months. During each appointment, an evaluation of the thyroid hormone profile and voice and measurements of total blood and ionized calcium, were conducted. The patients were categorized into three groups: group A, characterized by normocalcemia; group B, consisting of hypocalcemic individuals with euparathyroidism; and group C, comprising hypocalcemic individuals with hypoparathyroidism.

In this study, the levels of total and ionized calcium after surgery were utilized as a means of

screening for postoperative hypocalcemia before the manifestation of any signs or symptoms associated with hypocalcemia. The study aimed to evaluate the parathyroid glands' functionality and forecast permanent hypocalcemia by measuring PTH levels in individuals diagnosed with hypocalcemia. The examination of clinicopathologic data and the comparison of values across various groups are essential in the identification of risk factors associated with the development of permanent hypocalcemia.

2.3. Statistical analysis of data

The data underwent analysis utilizing Microsoft Excel and SPSS software for Windows (version 1.0.0.137; SPSS Inc., Chicago, Illinois, USA). The continuous variables were expressed as the mean plus or minus the SD, a method used to evaluate the central tendency and dispersion of the data points relative to their average value.

3. Results

A retrospective analysis was conducted on a cohort of 30 individuals who had undergone complete thyroidectomy and bilateral central node dissection as part of their treatment for papillary thyroid cancer. The patients were then monitored to assess the occurrence of postoperative hypocalcemia.

The often employed primary surgical intervention consisted of extracapsular complete thyroidectomy, accompanied by a thorough dissection of the tracheo-esophageal groove. Throughout the procedure, diligent efforts were undertaken to identify and safeguard the vascularization of all parathyroid glands. The preservation of the parathyroid glands was performed in all cases. The patients' serum total and ionized calcium levels were assessed before the surgical procedure and then reevaluated on the first day following the operation.

After their surgical procedures, patients were subsequently scheduled for follow-up appointments at 1, 2, and 6 months. Those individuals who exhibited symptoms of hypocalcemia, in addition to having a total calcium level below 8.9 mg/dl (within the normal range of 8.9–10.1 mg/dl) or an ionized calcium level below 1 mM/l (within the normal range of 1–1.35 mM/l), were classified as having hypocalcemia. Furthermore, the level of PTH was assessed.

Patients diagnosed with hypocalcemia were prescribed a daily oral dosage of 2 g of calcium carbonate and 0.5 µg of oral 1,25-dihydroxycholecalciferol. In cases where additional treatment was required, intravenous administration of calcium gluconate was also provided.

Patients who exhibited a persistent need for calcium carbonate and oral 1,25-dihydroxycholecalciferol for a duration exceeding 3 months following the surgical procedure were classified as individuals experiencing permanent hypocalcemia (Table 1).

The study examined various clinicopathologic characteristics, such as the age and gender of patients, the presence of multiple lesions, the size of the tumor, the extent of extrathyroidal spread, the presence of lymphovascular invasion, the presence of comorbidities related to the thyroid, and the number of preserved parathyroid glands. A total of seven patients exhibited malignancies that were localized exclusively within the thyroid gland, whereas 21 patients displayed evidence of focal capsular invasion. Two individuals exhibited malignancies visibly infiltrating the capsule (Table 2).

The sample population included nine male individuals and 21 female individuals. The average age of the participants was 44.64 years (range: 18–70 years) with a SD of ±16.86 (Figs 1 and 2 and Table 3).

The patients were classified based on the TNM staging criteria, where 18 (60%) patients had tumors with a maximum diameter of less than or equal to 2 cm, and were categorized as T1 tumors. A total of nine (30%) patients were diagnosed with T2 tumors, characterized by a tumor size ranging from greater than 2–4 cm, and the absence of extrathyroid extension. A mere three cases, constituting 10% of the sample, exhibited tumor sizes above 4 cm without any discernible infiltration into the adjacent tissue (Fig. 3 and Table 4).

Table 1. Clinicopathological character of all patients.

Characteristics	n (%)
Mass size (mm)	19.96 ± 9.5
Multifocality	
Single	21 (70)
Multiple	9 (30)
Capsular invasion	
Invasive	2 (6.66)
Focally invasive	21 (70)
Noninvasive	7 (23.3)

Table 2. Demographic distribution of the studied patients.

	All patients (N = 30) [n (%)]
<45 years	12 (40)
≥45 years	18 (60)
Sex	
Males	9 (30)
Females	21 (70)
Left lobe	18 (60)
Right lobe	12 (40)

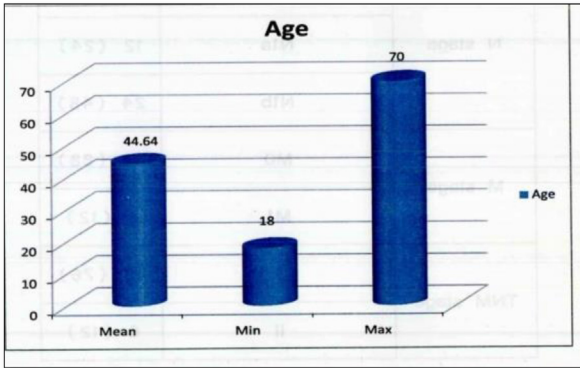


Fig. 1. Description of age in studied patients.

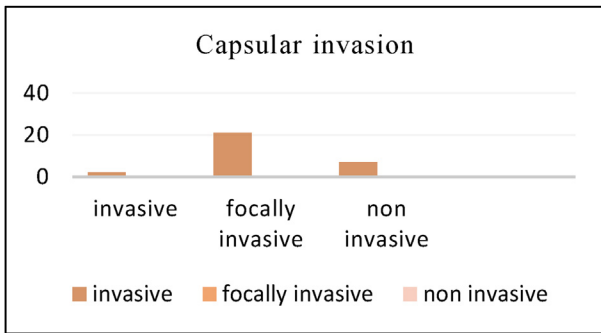


Fig. 2. Description of capsular invasion in studied patients.

Table 3. T staging among the studied patients.

T stage	n (%)
T1	18 (60)
T2	9 (30)
T3	3 (10)

Nine patients exhibited the absence of central node deposits (NOa), whereas six patients presented with positive central lymph nodes (N1a). Metastatic deposits were observed in central and lateral lymph nodes (N1b) among the remaining 15 patients. Out of the total sample size, three patients were diagnosed with metastatic disease (M1), while the remaining 27 patients did not exhibit any signs of metastasis (MO) (Figs 4–6).

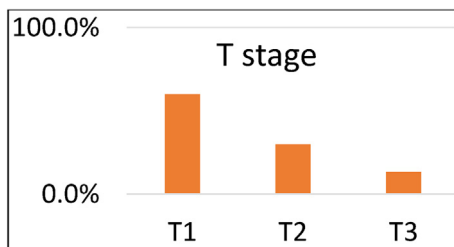


Fig. 3. T staging among the studied patients.

Table 4. Tumor character.

Characteristics	n (%)
N stage	
N0a	9 (30)
N1a	6 (20)
N1b	15 (50)
M stage	
M0	27 (90)
M1	3 (1)
TNM stage	
I	21 (70)
II	6 (20)
III	3 (10)

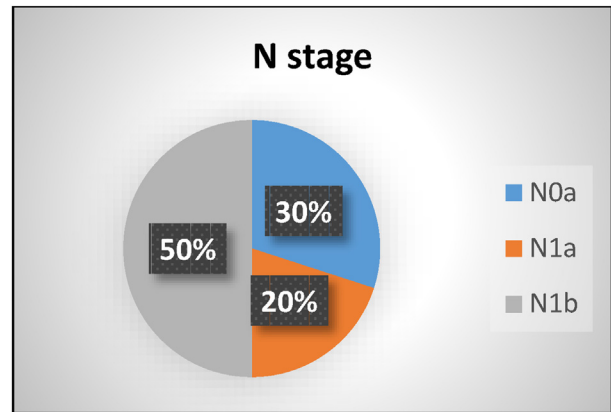


Fig. 4. N staging among the studied patients.

After staging all the patients according to the TNM staging system, 21 patients were defined as stage I. Six patients were defined as stage II and three patients as stage III (Fig. 7).

All efforts were spent to preserve all the parathyroid glands. In 21 patients, all the four glands were preserved, while in seven patients, one gland was incidentally removed, and in two patients, all parathyroid gland was incidentally removed (Table 5).

The present investigation involved the evaluation of hypocalcemia through the measurement of total

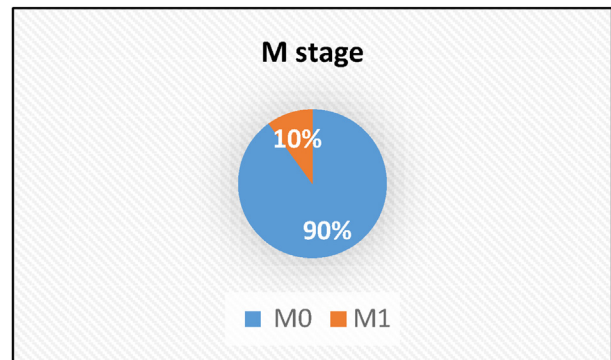


Fig. 5. M staging among the studied patients.

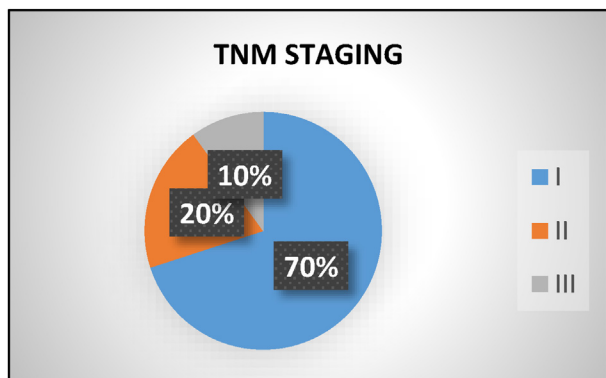


Fig. 6. TNM staging among the studied patients.

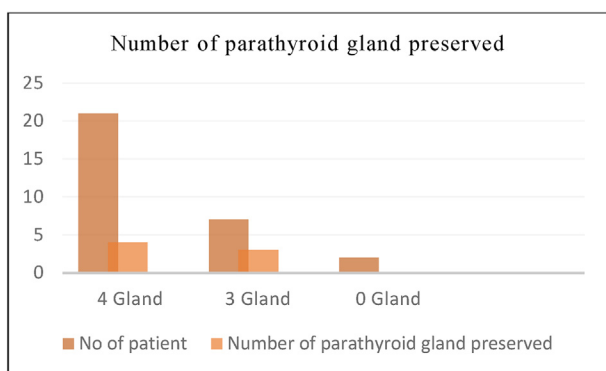


Fig. 7. Number of parathyroid glands preserved about the patient.

and ionized calcium levels following surgical procedures, with subsequent comparison to preoperative values. A study was measured on PTH in cases demonstrating hypocalcemia.

A total of 30 patients were enrolled in this trial, all of whom underwent complete thyroidectomy with bilateral central neck dissection. The dissection procedure was conducted with meticulous care to

prevent harm to any of the parathyroid glands and to preserve their vascular integrity.

A decrease in blood total and ionized calcium levels was observed in 15 individuals following surgery compared to their preoperative levels. Out of the total sample size of 15 patients, it was observed that nine patients maintained normocalcemia even after experiencing a decrease in serum calcium levels following the surgical procedure, as compared to their preoperative levels. The remaining six patients had early postoperative hypocalcemia and underwent measurement of their PTH levels. Remission was observed in three individuals presenting with early hypocalcemia. In contrast, three other patients exhibited a prolonged dependence on oral vitamin D and calcium supplements for a duration beyond 6 months, satisfying the criteria indicative of persistent hypocalcemia.

According to the methodology employed in this study, the participants and the subjects were classified into three discrete categories. Group A consisted of 24 normocalcemic patients, whereas group B consisted of three persons with euparathyroid hypocalcemia. Finally, group C consisted of three patients who were diagnosed with hypoparathyroidism.

4. Discussion

Hypocalcemia is a notable complication that can occur following a complete thyroidectomy and central neck dissection surgery. The observed phenomenon can be ascribed to the physical proximity of the gland that produces thyroid hormone and the parathyroid gland, both of which possess a vital function in the regulation of blood calcium levels by means of PTH secretion.

Table 5. Patient groups (univariate analysis).

	Group A	Group B	Group C
Age (mean in years)	42 ± 13.71	45.4 ± 14.4	66.5 ± 2.5
Female: male ratio	3.5 : 1	4 : 1	1 : 1
Tumor size (mm)	19.55 ± 9	19.4 ± 11.9	25 ± 5
Multifocality			
Single	18	1	2
Multiple	6	2	1
Extrathyroid extension			
Invasive	—	—	2
Focally invasive	19	1	1
No	5	2	—
TNM stage			
I	18	1	2
II	4	2	—
III	2	—	1
Preoperative calcium level			
Total	9.53 ± 0.38	8.98 ± 0.12	9.15 ± 0.25
Ionized	1.07 ± 0.11	0.92 ± 0.04	1.295 ± 0.005

PTH is a peptide composed of 84 amino acids and is vital in regulating the levels of calcium and phosphate in the bloodstream. The compound demonstrates a relatively short half-life of roughly 5 min. The regulation of secretion is contingent upon the level of ionized calcium in the bloodstream, which engages with a calcium-sensing receptor situated on the cell membrane of the parathyroid glands. The stimulation of the G-protein related receptor results in the inhibition of PTH release and a reduction in the calcium levels in the bloodstream. An inverse sigmoidal relationship can be observed regarding serum ionized levels of calcium and PTH.⁹

Iatrogenic injury to the parathyroid glands is an unexpected outcome that may occur as a result of complete thyroidectomy. The assessment of parathyroid gland function and identification of patients at risk for hypocalcemia can be effectively achieved through the sensitive and specific measurement of serum PTH immediately following surgical procedures.¹⁰

The administration of calcium in combination with activated vitamin D, namely calcitriol, has demonstrated a reduction in the incidence of symptomatic hypocalcemia in cases when the postoperative PTH level is low.¹¹

Given the awareness among surgeons regarding the potential danger associated with surgery, it is common practice to administer either calcium or calcitriol empirically to patients as a preventive measure against the development of symptoms. Although this supplement can effectively alleviate symptoms in patients, it presents challenges in accurately discerning those with transitory hypoparathyroidism from those without, only relying on calcium levels, symptoms, or the necessity for supplementing.¹²

A significant proportion of individuals with parathyroid dysfunction after thyroidectomy typically exhibit a restoration of normal parathyroid function within a very short timeframe, typically ranging from a few weeks to 1 month following the surgical procedure.¹³

Nevertheless, a dearth of agreement may be observed within the academic literature about the optimal definition of parathyroid gland function recovery. In certain investigations, patients are classified as euparathyroid once their serum PTH levels have reached a minimum of 10 pg/ml, provided that they do not exhibit signs of hypocalcemia.¹⁴

The attention of certain individuals is directed towards the administration of medication, while the restoration of parathyroid gland function is taken

into account when the patient reaches a point where therapeutic calcium or calcitriol supplementation is no longer necessary to prevent symptoms associated with hypocalcemia.¹⁵

One additional approach to delineating the restoration of parathyroid gland functionality involves the integration of both factors, namely the attainment of serum PTH levels within the normal range and the discontinuation of calcium or calcitriol treatment.¹⁶

Based on the findings of Lombardi *et al.*,¹⁷ it was determined that PTH levels measuring below 10 pg/ml, assessed 4 h postsurgery, demonstrated limited reliability in predicting hypocalcemia among 13.4% of the individuals. Among this group, 2.1% experienced symptoms associated with hypocalcemia. Patients who experience substantial hypocalcemia and symptoms may exhibit postoperative PTH readings that appear to be within the normal range, but this can be misleading.¹⁸

Moreover, many temporal markers have been employed to ascertain the appropriate classification of postoperative hypoparathyroidism as a permanent condition. There is a prevailing belief among certain individuals that in cases where restoration of functionality has not been observed within a 6-month timeframe, postoperative damage to the parathyroid gland is deemed irreversible.¹⁹ Meanwhile, some individuals establish the concept of permanence as being 1 year following the surgical procedure.¹⁵

Relative hypoparathyroidism, also known as parathyroid insufficiency, is characterized by the presence of clinical signs of hypoparathyroidism that necessitate medical intervention despite laboratory measurements falling within the normal range.²⁰

Group B individuals are characterized by the presence of relative hypoparathyroidism.

The findings suggest that postoperative hypocalcemia is primarily caused by damage to the parathyroid glands during surgery. The degree of parathyroid dysfunction and resultant transitory hypocalcemia in instances of mild trauma, whereby the bloodstream to the parathyroid glands continues unaffected, is contingent upon the severity of the damage.

One of the limitations of this study is the absence of preoperative measurement of PTH, which prevented the assessment of the decrease in postoperative PTH levels. The measurement of serum albumin was not conducted, resulting in the inability to determine the corrected calcium level.

The measurement of serum magnesium level was not conducted despite the acknowledged involvement of magnesium in the release of PTH.

4.1. Conclusion

The surgical method is considered the primary risk factor for the development of post-thyroidectomy hypocalcemia. Both meticulous dissection techniques aimed to reserve the parathyroid glands are equally important through the conservation of blood flow and the meticulous treatment of parathyroid tissue. Additional risk variables encompass advanced age, substantial tumor size, and progression to later stages.

Ethical consideration

The ethical committees of the Faculty of Medicine, Department of Surgical Oncology, El Sayed Galal University Hospital and El Hussien University Hospitals, granted official approval. Approval from the medical faculty's ethical committee is detailed in writing. Consent was obtained from all participants subsequent to their being properly informed of the study's aims, methodology, & applicable objectives.

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Conflicts of interest

There are no conflicts of interest.

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