Case study

PREDICTIVE FACTORS OF POST-THYROIDECTOMY HYPOCALCEMIA: EXPERIENCE OF THE SURGERY A DEPARTMENT AT IBN SINA HOSPITAL.

Abstract

Summary:

Post-thyroidectomy hypocalcemia remains a frequent complication, hence the need to find predictive factors to improve preoperative risk assessment and reduce complications. This retrospective study carried out in the Surgical Department A of Ibn Sina Hospital from 2007 to 2022, examined 539 cases of thyroidectomy. The aim is to identify factors influencing postoperative hypocalcemia, whether transient or permanent. Parameters include age, sex, medical history, preoperative symptoms, thyroid hormone levels, diagnosis, type of surgery, detection of parathyroid gland, incidentaloma, lymph node dissection, and operator expertise. The results indicate that 31.91% of patients developed postoperative hypocalcemia, 6.39% of whom required prolonged calcium supplementation. Significantly associated factors were female gender, preoperative hyperthyroidism, total thyroidectomy, accidental parathyroidectomy, multinodular goiter, whether or not parathyroid glands were detected, parathyroid incidentaloma, surgical expertise and hematoma or haemorrhage requiring revision surgery. Surgical history, hypertension, and diabetes did not have a statistically significant impact. Understanding these predictive factors is crucial for refining surgical strategies, optimizing patient care, and potentially reducing the hospitalization costs associated with post-thyroidectomy hypocalcemia. Further studies should explore the interaction between these factors and refine risk prediction models to improve patient outcomes.

Keywords: prevention, thyroidectomy, hypocalcemia, thyroid surgery.

Introduction

The occurrence of hypocalcemia after thyroidectomy is partly linked to revascularization or accidental excision of the parathyroid glands during the operation, as they secrete parathyroid hormone, which helps to regulate blood calcium levels [1].

Post-thyroidectomy hypocalcemia can be profound but is reversible in many cases. It can be transient or permanent and can lead to high hospitalization costs in the event of calcium supplementation. It can be either asymptomatic or symptomatic, ranging from minor signs to major complications leading to hypocalcaemic tetany. It is the most common complication of thyroidectomy [2].

Many endocrine surgeons are interested in early prediction of hypocalcemia to prevent serious complications and possibly start treatment to reduce the length of hospital stay.

This retrospective observational study aimed to prevent or develop a better management strategy for hypocalcemia in patients undergoing different types of thyroidectomy for different thyroid pathologies, based on factors that could be used as predictors of postoperative, transient, or permanent hypocalcemia.

Methodology

We conducted a retrospective study using patients' medical records and computerized data where available, from January 2007 to December 2022, of patients undergoing thyroid surgery in the "A" surgery department of Ibn Sina Hospital for various thyroid pathologies.

Patients with concomitant parathyroid disease and renal failure were excluded from this study.

The parameters studied were: age, sex, medical history and history of thyroid surgery, pre-operative symptoms, pre-operative TSH level, diagnosis, type of surgery, detection of parathyroid glands during surgery, discovery of parathyroid incidentaloma, type of lymph node dissection and quality of surgeon.

The group of postoperative hypocalcemia was correlated with the different parameters studied to label those that were statistically significant.

Qualitative variables are represented by frequencies and percentages. Differences in frequencies between groups and the statistical significance of the different factors were calculated using Fisher's exact test or the CHI 2. Odds ratios and 95% CIs for each variable and a p-value < 0.05 were considered statistically significant.

Results

From January 2007 to December 2022, we compiled 539 records of patients who had undergone thyroid surgery in the "A" surgery department of the Ibn Sina Hospital in Rabat for various thyroid pathologies and who met our inclusion criteria.

Parameters correlated with the post-operative hypocalcemia group included age, sex, medical and surgical history, pre-operative symptoms, pre-operative TSH level, diagnosis, type of surgery, detection of parathyroid glands during surgery, discovery of parathyroid incidentaloma, type of lymph node dissection and quality of operator.

In our study, 172 patients (31.91%) developed postoperative hypocalcemia (i.e.<80 mg/l), including 11 with permanent hypocalcemia requiring indefinite calcium supplementation.

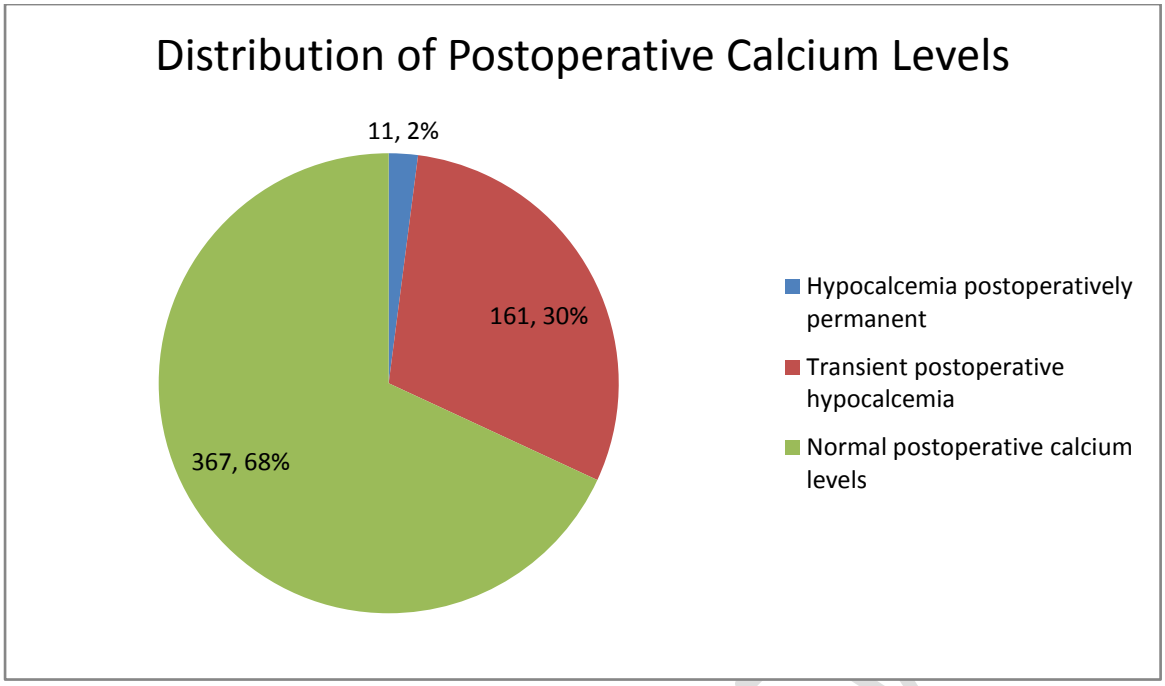

Fig 1. Distribution of Postoperative Calcium Levels

- Age:

The mean age of patients who developed postoperative hypocalcemia was 46.31 ± 13.7 years compared with 47.7 +/- 14.6 years for patients who did not develop hypocalcemia, with p = 0.477.

- Genre:

We found that 161 female patients (33.40%) versus 11 (19.29%) male patients developed postoperative hypocalcemia, with OR: 0.48, CI [0.24-0.95] and p = 0.031.

Table 1.Male and female patients developed postoperative hypocalcemia

	Post-operative hypocalcemia	Normal postoperative blood calcium levels	Total	khi-deux	Value of p
Women	161	321	482		
Men	11	46	57		
Total	172	367	539	4,67	0,031

- Previous thyroid-related surgery:

In our series, post-operative hypocalcemia was observed in 19 patients (24.67%) with a history of thyroidectomy, compared with 153 patients (33.11%) undergoing thyroidectomy for the 1st time, with p = 0.14. It was transient in 18 patients (23.37%) and permanent in 1 patient (1.29%). It was transient in 18 patients (23.37%) and permanent in 1 patient (1.29%).

- HBP

Of the patients with postoperative hypocalcemia, 22 (24.71%) were hypertensive compared with 150 (33.33%) who were not; p=0.11.Hypocalcemia was transient in 21 patients (23.59%); p=0.15. It was permanent in 1 patient (1.12%), p=0.50.

- Diabetes

Of 172 patients who developed post-operative hypercalcemia, 13 (27.08%) were diabetic versus 159 patients (0.32%) who were not (p=0.45). Hypocalcemia was transient in the 13 patients (p=0.45). There was no permanent hypocalcemia in diabetics (p=0.29).

- Diagnosis:

Post-thyroidectomy hypocalcemia was observed in 124 patients (35.63%) diagnosed as Multi-Nodular Goiter (MNG) versus 48 patients (25.13%) with another diagnosis, with p=0.012.

It was transient in 113 patients (32.47%) with p= 0.07 and permanent in 11 patients (3.16%).

None of the patients with another diagnosis developed permanent hypocalcemia, with p = 0.013.

Table 2. MNG and other diagnosis developed postoperative hypocalcemia

	Post-operative hypocalcemia	Normal post-operative blood calcium levels	Total	Chi-square	Value of p
MNG	124	224	348		
Other diagnosis	48	143	191		
Total	172	367	539	6,26	0,012

- Presence of pre-operative symptoms:

Concerning preoperative symptoms, of the 172 patients who developed postoperative hypocalcemia, 152 (34.78%) had preoperative symptoms versus 20 patients (19.60%) who had no preoperative symptoms, with p= 0.003.

Transient hypocalcemia was observed in 143 symptomatic patients (32.72%) with p=0.003 versus 9 cases of permanent hypocalcemia (2.05%) with p=0.94.

Table 3.Presence of pre-operative symptoms

	Post-operative hypocalcemia	Normal post-operative blood calcium levels	Total	Chi-square	Value of p
Pre-operative symptoms	152	285	437		
No pre-operative symptoms	20	82	191		
Total	172	367	539	8,76	0,003

- TSHus

Of the 172 patients who developed post-thyroidectomy hypocalcemia, 64 (36.15%) had preoperative hyperthyroidism compared with 108 patients (29.83%) with normal TSH levels, with p<0.001.

Transient hypocalcemia was observed in 61 patients (34.46%) with p<0.001. It was permanent in 3 patients (1.69%) with p=0.13.

Table 4.Transient hypocalcemia

	Post-operative hypocalcemia	Normal post-operative blood calcium levels	Total	Chi-square	Value of p
Pre-operative hyperthyroidism	64	3	67		
TSH normal	108	364	472		
Total	172	367	539	142,49	< 0,001

- Type of intervention

Two patients (3.57%) developed postoperativehypocalcemia after isthmolobectomy, compared with 170 patients (35.19%) in the second group who had bilateral surgery, p<0.001.

Among patients who underwent total thyroidectomy, it was transient in 159 (32.92%) and permanent in 11 (2.27%) with p<0.001.

None of the patients who underwent isthmolobectomy developed permanent hypocalcemia, with p = 0.25

Table 5.isthmolobectomy developed permanent hypocalcemia

	Post-operative hypocalcemia	Normal post-operative blood calcium levels	Total	Chi-square	Value of p
Isthmolobectomy	2	56	58		
Total thyroidectomy	170	311	481		
Total	172	367	539	24,23	< 0,001

- Detection of parathyroid glands

In our study, 481 patients (89.23%) underwent total thyroidectomy. Of the 445 patients who had more than 2 parathyroid glands seen during the operation, 158 (35.50%) developed postoperative hypocalcemia versus 12 patients (35.29%) of the 34 patients who had less than 2 parathyroid glands seen during the operation, with p<0.001.

Table 6.parathyroid glandsdeveloped postoperative hypocalcemia

	Post-operative hypocalcemia	Normal post-operative blood calcium levels	Total	Chi-square	Value of p
More than 2 parathyroid glands seen	158	289	445		
Less than 2 parathyroid glands seen	14	78	92		
Total	172	367	539	14,41	< 0,001

Of the 56 patients (10.38%) who underwent isthmolobectomy, 1 patient (2.38%) out of the 42 in whom both parathyroid glands were seen, developed hypocalcemia versus 1 patient (9.09%) out of the 11 patients who had only 1 parathyroid gland seen during surgery, with p = 0.4.

- Parathyroid incidentaloma:

Among patients with postoperative hypocalcemia, 4 (80%) had a parathyroid incidentaloma out of the 5 incidentalomas, compared with 168 (31.46%) out of 534 without incidentaloma, with p=0.02.

Table 7.Parathyroid incidentaloma

	Post-operative hypocalcemia	Normal post-operative blood calcium levels	Total	Chi-square	Value of p
Parathyroid incidentaloma	4	1	5		
No parathyroid incidentaloma	168	366	534		
Total	172	367	539	5,37	0,02

-Inadvertent parathyroidectomy and self-implantation of parathyroid glands:

Of the 42 patients who underwent inadvertent parathyroidectomy, 18 patients (42.86%) developed post-operative hypocalcemia compared with 154 patients (30.98%) without inadvertent removal of the parathyroid glands, with p=0.11.

Postoperative hypocalcemia was observed in 17 patients (42.50%) out of the 40 patients who benefited from the parathyroid gland autograft versus 155 patients (31.06%) who did not, with p=0.13. These were transient hypocalcemia

- Dissection:

Postoperative hypocalcemia was observed in 8 patients (38.09%) out of the 21 who underwent anterior cervical dissection versus 8 patients (36.36%) out of the 22 who underwent posterolateral neck dissection, with p=0.9. The hypocalcemia was transient.

Eleven patients (36.66%) out of the 30 who underwent bilateral cervical dissection developed postoperative hypocalcemia, whereas 5 patients (22.72%) out of the 22 who underwent unilateral cervical dissection developed postoperative hypocalcemia, with p=0.28. These were transient hypocalcemia.

- Surgical expertise:

Of the 51 surgical procedures performed by residents, 10 (19.60%) developed postoperative hypocalcemia, compared with 162 patients (33.19%) operated on by senior surgeons (p=0.048).

Table 8.Surgical procedures developed postoperative hypocalcemia

	Post-operative hypocalcemia	Normal post-operative blood calcium levels	Total	Chi-square	Value of p
Resident	10	41	51		
Surgeon	162	326	488		
Total	172	367	539	3,92	0,048

Transient hypocalcemia was observed in 9 patients (17.64%) operated on by residents versus 152 patients (10.65%) operated on by chief surgeons, with p=0.045.

Permanent hypocalcemia was observed in 1 patient (1.96%) whose operation was performed by residents versus 10 patients (0.20%) whose operations were performed by chief surgeons, with p=0.95.

- Post-thyroidectomy hematomas and haemorrhages requiring repeat surgery:

Of the 10 patients who required emergency reoperation, 6 (60%) developed postoperative hypocalcemia after the emergency reoperation, compared with 166 patients (31.38%) who did not undergo any reoperation (p=0.054).

Table 9.Post-thyroidectomy hematomas and haemorrhages requiring repeat surgery

	Post-operative hypocalcemia	Normal post-operative blood calcium levels	Total	Chi-square	Value of p
Surgical revision	6	4	10		
No repeat surgery	166	363	529		
Total	172	367	539	3,7	0,054

Discussion

In this study; female gender, preoperative hyperthyroidism, preoperative hypocalcemia, total thyroidectomy, inadvertent para thyroidectomy, multinodular goiter, preoperative hyperthyroidism, number of parathyroid glands detected, parathyroid incidentaloma, surgical expertise, hematoma or haemorrhage, were statistically significant variables.

On the other hand, variables that were significant in other studies were not significant in ours. These included: old age, Graves' disease, thyroid cancer, previous cervical dissection, and thyroid volume.

We also found that hypertension and diabetes were not significant variables.

Numerous studies have evaluated possible risk factors for post-thyroidectomy hypocalcemia, some of which have been generally accepted.

However, establishing these risk factors remains a challenge. In our study, we evaluated the biological, clinical, and surgical factors that may influence the development of post-thyroidectomy hypocalcemia.

In our series, 31.91% of patients developed postoperative hypocalcemia, 93.60% of whom recovered before 12 months (transient hypocalcemia), without needing replacement therapy for at least 1 month, while 6.39% needed to maintain calcium supplementation for more than 12 months after surgery (permanent hypocalcemia). The British Association of Endocrine and Thyroid Surgeons audit [3] reported rates of 27.4% and 12.1%. The reported rate of postoperative hypocalcemia varies from study to study due to a lack of consensus on the definition and criteria for postoperative hypocalcemia[4].

- Type

In the present study, the sex ratio was disproportionately high (482 women versus 57 men [89.42% versus 10.58%]), and postoperative and transient hypocalcemia was significantly more frequent in women in the statistical analyses (p=0.03) and similar to the literature [5;3;6].

A priori, we relate these results to the fact that in our series, as in several others, women are more exposed than men to developing thyroid pathology due to several causes.

However, in rare cases, some studies have reported conflicting results regarding the female sex as a risk factor for post-thyroidectomy hypocalcemia [65]. In our study, we did not control for possible confounding factors that could partly explain our results because the female sex has various factors that may interact with calcium levels. Women are more likely to have a disease associated with a variety of hormones, such as menopausal syndrome, osteoporosis, and vitamin D deficiency. Thus, assessments of bone mineral density, menstrual status, and other hormone levels may be necessary [8; 9]. However, preoperative vitamin D and preoperative bone mineral density were not measured in our study.

Furthermore, as shown in previous studies, vitamin D levels are lower in women [10]. It is thought that preoperative vitamin D levels may predict post-thyroidectomy hypocalcemia [8]. A Moroccan study by Allali F [9] of 415 women aged between 24 and 77 showed that vitamin D deficiency (VDD) affects more than 90% of Moroccan women. In Morocco, vitamin D deficiency is linked to a lifestyle that does not favour exposure to the sun, particularly in clothing covering the whole body, and the lack of outdoor activities that limit exposure to the sun.

- Preoperative hyperthyroidism:

In our study population, preoperative hyperthyroidism was significantly associated with transient hypocalcemia (p<0.001).

This result correlates with the literature which has found that the incidence of transient hypocalcemia appears to be higher in thyrotoxic patients compared with euthyroid patients undergoing thyroidectomy for other benign non-toxic thyroid nodules. [11].

In addition, a diagnosis of hyperthyroidism is independently associated with a difficult thyroidectomy [12; 13] which may be due to hypervascularisation of the thyroid gland during hyperthyroidism.

Other studies suggest that the risk of hypocalcemia is not reduced by correcting hyperthyroidism a few weeks before thyroidectomy [14]. It is correlated with serum levels of free thyroxine before treatment [15] and with markers of bone turnover, such as serum alkaline phosphatase [16] and urinary hydroxyproline [17]. Euthyroidism before surgery and, more importantly, a prolonged period of euthyroidism before surgery may prevent the occurrence of postoperative hypocalcemia in patients with hyperthyroidism.

- Type of intervention:

In this case series, our patients were divided into 2 groups according to the type of procedure; group 1 comprised patients undergoing isthmolobectomy, and group 2 comprised patients undergoing total thyroidectomy.

We found the rate of post-operative and transient hypocalcemia to be significantly higher in the 2nd group of patients who had undergone total thyroidectomy ($p<0.001$).

This may seem like an obvious result, as during isthmolobectomy, only one side is explored, exposing only 2 parathyroid glands while the contralateral lobe remains intact. It is known that only one functional gland is capable of maintaining calcium metabolism at normal values [18].

- Dissection:

In this study, central cervical dissectionand lateral cervical dissection (LCC) were found to be insignificant ($p=0.28$), whereas the extent of anterior cervical dissection was significant in the development of post-thyroidectomy hypocalcemia ($p=0.038$).

Patients who underwent total thyroidectomy had a higher rate of transient post-operative hypocalcemia than patients who underwent isthmolobectomy.

Considering the general anatomy and location of the parathyroids, it is less likely that LCC affects the development of hypoparathyroidism. In a retrospective study of 1030 patients who underwent total thyroidectomy, they found that the extent of the was significant in the same way as our results [19].

- Identification of parathyroids:

In our study, Para identification was significantly associated with the occurrence of transient or permanent hypocalcemia ($p<0.001$). However, patients undergoing bilateral surgery who had fewer than 2 parathyroid glands identified during surgery had a lower incidence of transient hypocalcemia post-thyroidectomy than those who had more than 2 parathyroid glands seen during surgery (34 versus 445). This correlates with a study of 569 patients which found that when the extracapsular technique was adopted during total thyroidectomy, identifying fewer parathyroid glands in their orthotopic positions not only reduced the risk of temporary and prolonged hypoparathyroidism but also shortened recovery from prolonged hypoparathyroidism [20]. Some authors suggest that this is due to the risk of injury inherent in parathyroid manipulation [21]. However, there is no consensus on the recommendation to identify parathyroid glands to retain them or on the minimum number of glands to retain [22]. In a retrospective study of 254 patients, the authors suggest that careful dissection of the thyroid capsule as close as possible to the thyroid parenchyma and identification of the paras before ligation of the inferior thyroid artery are important both to avoid damage to the structure and vascularization and to avoid accidental removal with the thyroid lobe [23].

- Parathyroid incidentaloma

We found that 5 patients (0.92%) had a parathyroid incidentaloma discovered during the operation. Four of them (80%) presented with postoperative hypocalcemia, with p=0.02. It was transient in 3 patients (75%), with p=0.13. And permanent in 1 patient (25%), with p=0.004. Our results are superior to those reported by I. Benabbad et al. in a prospective study, with an incidence of 1% of primary hyperparathyroidism revealed by post-thyroidectomy hypocalcemia[24]. Carnaille et al report an incidence of 0.6% [24;25] in their study, Hellman et al have an incidence of 2% [26],and in the most recent study (Abboud et al.) an incidence of 1.9% [27].

Indeed, in the absence of major recurrence risk, we decided to resect any parathyroid incidentaloma to avoid the risks of subsequent surgery, as incidentally discovered parathyroid hyperplasia could represent a pre-pathological state leading to HPTP [24].

- Age:

In this study, we found no significant difference in mean age between patients who developed postoperative hypocalcemia and those who did not (46.31 ± 13.7 versus 47.7 ± 14.6 years, p= 0.477). The same was true for transient hypocalcemia (49.2+/- 13.7 years versus 47.5 +/- 14.5 years, p=0.234) and permanent hypocalcemia (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 (48.5 ± 14.3 years) is much younger than in the literature [23; 28]. However, there are studies similar to ours that have noted a limited association between advanced age and thyroidectomy outcome. A prospective study [29] of a population of 85 patients and 44 thyroidectomised patients aged 21-35 years versus ≥ 65 years respectively, showed no difference in complication rates between younger and older patients. The influence of age on post-thyroidectomy hypocalcemia still needs to be clarified given other confounding patient and disease factors. Advanced age is associated with vitamin D deficiency [30], probably due to reduced skin 7- dihydrocholesterol, decreased renal 1α hydroxylase activity, and reduced calcium absorption [31].

- History of thyroid surgery:

Contrary to some studies which conclude that totalization may increase postoperative complications such as hypoparathyroidism [32]. In our study, we found an increased incidence of postoperative, transient, and permanent hypocalcemia in patients undergoing thyroidectomy for the 1st time, but it was not statistically significant (p = 0.14). Similarly, to our results, a retrospective study carried out at the McGill University Thyroid Cancer Centre, Montreal, Quebec, Canada, reported that the occurrence of transient hypocalcemia was significantly lower in the totalization group than in the total thyroidectomy group. And that transient hypocalcemia occurred in 1.5% of patients after totalization and 12.5% after total thyroidectomy but there was no significant difference in the occurrence of permanent hypocalcemia between the two groups [33].

In the case of totalization, the devitalized parathyroid may be revascularised before the second operation because of the time lag between thyroidectomy for totalization and the 1st operation. This may reduce the rate of post-thyroidectomy hypocalcemia[34].

Some research suggests that totalization may increase postoperative complications such as hypoparathyroidism, particularly when performed by inexperienced surgeons [35]. It is known that sufficiently experienced surgeons can perform iterative thyroidectomy with low morbidity [36]. The difficulty in performing thyroidectomy is due to postoperative fibrosis and therefore the increased risk of damage to the parathyroid glands [40]. They recommend that the final thyroidectomy should be performed within 10 days or at least 3 months after the first operation to avoid postoperative fibrosis in the surgical field [36; 37].

- Hypertension and diabetes

Regarding the relationship between the occurrence of postoperative, transient, and permanent hypocalcemia and hypertension, we found no significant difference ($p = 0.11$). We did not find any information on the relationship between hypertension and post-thyroidectomy hypocalcemia in the literature. However, a retrospective study of a sample of 2559 patients found that hypertension was related to the occurrence of another complication of thyroidectomy; postoperative hematomas. Their study found that 16 of 32 patients (50%) who underwent revision surgery had hypertension; the incidence of hematomas was 2.09% in hypertensive patients and 0.89% in patients without hypertension ($p<0.05$) [38]. In our study, none of the patients who developed hematomas or haemorrhages had hypertension.

The same result was observed about diabetes; there was no significant difference between diabetic and non-diabetic patients about the occurrence of postoperative ($p=0.45$), transient ($p=0.45$), and permanent ($p=0.29$) hypocalcemia. No information was found regarding the relationship between diabetes and post-thyroidectomy hypocalcemia.

- Surgical expertise:

In our study, we found that there was a significant difference in postoperative hypocalcemia between procedures performed by senior surgeons and residents ($p = 0.047$). We found that post-thyroidectomy hypocalcemia was more prevalent with surgeries performed by senior surgeons (33.19% versus 19.60%). This may be because senior surgeons performed many more procedures than the residents they supervised.

In the literature, the surgeon's experience is relevant to avoid post-thyroidectomy complications in general. A multicenter prospective cross-sectional study found that patients had an increased risk of permanent complications after thyroidectomy performed by less experienced surgeons and by those who had been practising for 20 years or more, suggesting that surgeons aged 35-50 years provided the safest care [39].

Conclusion

In this retrospective study conducted over 16 years at Ibn Sina Hospital in Rabat, surgery department "A" looked at the results of thyroid surgery. Several patient-related clinical and surgical risk factors for post-thyroidectomy hypocalcemia were identified. Notable predictors included preoperative hyperthyroidism, total thyroidectomy, number of parathyroid glands detected, preoperative hypocalcemia, and female gender. The results suggest systematic measurement of preoperative calcium levels for all patients undergoing thyroidectomy and preoperative vitamin D assessment for women. Calcium and vitamin D supplementation for patients with risk factors could prevent post-thyroidectomy hypocalcemia. Finally, the experience of the lead surgeon and a meticulous approach to thyroidectomy could significantly reduce the frequency of postoperative hypocalcemia.

References

1- Claire Nominé. How to predict the occurrence of symptomatic hypocalcemia after total thyroidectomy? Sciences du Vivant [q-bio]. 2013. HAL-01732233

2- Management and incidence of hypocalcemia after total thyroidectomy. M.Masmoudi*a(Dr), N.Ben Hamidaa(Dr), B.Zantourb(Dr), A.Zaydia(Dr), S.Jellelia(Dr), K.Mighria(Dr), N.Drissa(Pr) ENT and CCF Department, Mahdia, TUNISIA ; Endocrinology Department, Mahdia, TUNISIA

3- Chadwick D, Kinsman R, Walton P, Systems DC. The British Association of Endocrine and Thyroid Surgeon Fourth National Audit. Dendrite Clinical Systems Ltd: Henley-on-Thames, 2012.

4- Mehanna HM, Jain A, Randeva H, Watkinson J, Shaha A. Postoperative hypocalcemia difference a definition makes. Head Neck. 2010 Mar; 32(3):279-83. doi: 10.1002/hed.21175.

5- Cho.JN, Park.WS, Min. SY.Predictors.and.risk.factors.of hypoparathyroidism after total thyroidectomy. Int J Surg. 2016 Oct; 34: 47-52. doi: 10.1016/j.ijsu.2016.08.019. Epub 2016 Aug 20.

6- Sands N.B, Payne R.J, Côté V, Hier MP, Black MJ, Tamilia M, Female gender as a risk factor for transient post-thyroidectomy hypocalcemia, Otolaryngol.--Head Neck Surg. Off. J. Am. Acad. Otolaryngol. -Head Neck Surg. 145 (2011) 561-564. doi:10.1177/0194599811414511.

7- Sitges-Serra A, Ruiz S, Girvent M, Manjón H, Dueñas J.P, Sancho J.J, Outcome of protracted hypoparathyroidism after total thyroidectomy. Br J Surg. 2010 Nov;97(11):1687-95. doi: 0.1002/bjs.7219.

8- Kirkby-Bott J, Markoqiannakis H, Skandarajah A, Cowan M, Fleming B, Palazzo F. Preoperative vitamin D deficiency predicts postoperative hypocalcemia after total thyroidectomy. World. J. Surg. 2011, (324-30). doi:10. 1007/s00268-010-0872-y.

9- Allali F, El Aichaoui S, Khazani H, Benyahia B, Saoud B, El Kabbaj S, Bahiri R, Abouqal R, Hajjaj-Hassouni N. High Prevalence of Hypovitaminosis D in Morocco: Relationship to Lifestyle, Physical Performance, Bone Markers, and Bone Mineral Density. Semin Arthritis Rheum , 2009. doi:38:444-51.

10- Yamashita H1, Noguchi S, Murakami T, Uchino S, Watanabe S, Ohshima A, Kawamoto H, Toda M, Yamashita H. Calcium and its regulating hormones in patients with Graves disease: sex differences about postoperative tetany. Eur J Surg 2000. doi; 166: 924-928.

11- See.AC, Soo. KC.Hypocalcemia following thyroidectomy for thyrotoxicosis. Br J Surg. 1997 Jan;84(1):95-7.

12- Pattou F, Combemale F, Fabre S, Carnaille B, Decoulx M, Wemeau J. L, Racadot A, Proye C, Hypocalcemia following Thyroid Surgery: Incidence and Prediction of Outcome, World J. Surg. 22 (1998) 718-724. doi:10.1007/s002689900459.

13- Mok VM, Oltmann SC, Chen H, Sippel RS, Schneider DF. Identifying predictors of a difficult thyroidectomy. J Surg Res. 2014. doi;190:157- 163.

14- Laitinen, O. Hypocalcemia after thyroidectomy. Lancet. 1976 Oct 16 doi;2(7990):859-60

15- McHenry CR, Speroff T, Wentworth D, Murphy T. Risk factors for postthyroidectomy hypocalcemia. Surgery. 1994 Oct. doi;116(4):641-7.

16- Demeester-Mirkine N, Hooghe L., Van Geertruyden J, De Maertelaer V. Hypocalcemia after thyroidectomy. Arch Surg. 1992 Jul;127(7):854-8.

17- Witteveen JE, van Thiel S, Romijn JA, Hamdy NA. Hungry bone syndrome: still a challenge in the postoperative management of primary hyperparathyroidism: a systematic review of the literature. Eur J Endocrinol. 2013 Feb 20;168(3):R45-53. doi: 10.1530/EJE-12-0528.

18- Herranz,.González-Botas. J, Lourido Piedrahita.D Hypocalcemia after total thyroidectomy: incidence, control, and treatment. Acta Otorrinolaringol Esp. 2013 Mar-Apr;64(2):102-7. doi:10.1016/j.otorri.2012.09.001. Epub 2012 Oct 31.

19- Cho J. N, ParkW. S, Min S. Y. Predictors and risk factors of hypoparathyroidism after total thyroidectomy. Int J Surg. 2016 Oct;34:47-52. doi: 10.1016/j.ijsu.2016.08.019. Epub 2016 Aug 20.

20- Lang BH, Chan DT, Chow FC. Visualizing fewer parathyroid glands may be associated with lower hypoparathyroidism following total thyroidectomy. Langenbecks Arch Surg. 2016 Mar; 401(2):231-8. doi: 10.1007/s00423-016-1386-3. Epub 2016 Feb 19.

21- Pfleiderer AG, Ahmad N, Draper MR, Vrotsou K, Smith WK. The timing of calcium measurements helps to predict temporary and permanent hypocalcemia in patients having completion and total thyroidectomies. Ann R Coll Surg Engl. 2009. doi;91: 140-6.

22- Glinoer D, Andry G, Chantrain G, Samil N. Clinical aspects of early and late hypocalcemia after thyroid surgery. Eur J Surg Oncol. 2000. doi; 26:571-7.

23- Grogan RH, Mitmaker EJ, Hwang J, Gosnell JE, Duh QY, Clark OH, Shen WT. A population-based prospective cohort study of complications after thyroidectomy in the elderly. J Clin Endocrinol Metab. 2012 May; 97(5):1645-53. doi: 10.1210/jc.2011-1162. Epub 2012 Mar 14.

24- Benabbad I, Chraibi A, Iraqi H, Serji B, Mohsine R, Ifrine L, Belkouchi A, Bonnichon P, El Malki HO. Parathyroid incidentaloma. Literature review about three case reports. Ann Endocrinol (Paris). 2011 Feb ;72(1):30-3. doi: 10.1016/j.ando.2010.06.002.

25- Roh JL, Park CI. Intraoperative parathyroid hormone assay for management of patients undergoing total thyroidectomy. Head Neck 2006;28:990-7

26- Biswas NN, Chaudhury WA, Khan JA, Biswas AC, Arif KM, Ghosh S, Akter S Hypocalcaemic Tetany After Total Thyroidectomy Med. Coll. J. 2015; 10(2):59-62

27- Russ G, Bonnema SJ, Erdogan MF, Durante C, Ngu R, Leenhardt L. European thyroid association guidelines for ultrasound malignancy risk stratification of thyroid nodules in Adults: The EU-TIRADS. Eur Thyroid J (2017); 6, 225-37.

28- Mekel M, Stephen AE, Gaz RD, Perry ZH, Hodin RA, Parangi S. Thyroid surgery in octogenarians is associated with higher complication rates.Surgery. 2009.Nov;146(5):913-21.doi: 10.1016/j.surg.2009.05.004.

29- Seybt MW, Khichi S, Terris DJ. Geriatric thyroidectomy: safety of thyroid surgery in an ageing population. Arch Otolaryngol Head Neck Surg. 2009 doi;135:1041e1044.

30- Pearce SH, Cheetham TD. Diagnosis and management of vitamin D deficiency. BMJ 2010 doi; 340: b5664.

31- Erbil Y, Bozbora A, Ozbey N, Issever H, Aral F, Ozarmagan S, Tezelman S. Predictive value of age and serum parathormone and vitamin D3 levels for postoperative hypocalcemia after total thyroidectomy for nontoxic multinodular goiter. Arch Surg 2007, doi; 142: 1182-1187

32- Reeve T, Thompson NW. Complications of thyroid surgery: how to avoid them, how to manage them, and observations on their possible effect on the whole patient. World J Surg 2000 doi;24:971-5.

33- Merchavy S, Marom T, Forest VI, Hier M, Mlynarek A, McHugh T, Payne R. Comparison of the incidence of postoperative hypocalcemia following total thyroidectomy vs completion thyroidectomy. Otolaryngol Head Neck Surg 2015 doi: 10.1177/0194599814556250.

34- Park YM, Kim JR, Oh KH, Cho JG, Baek SK, Kwon SY, Jung KY, Woo JS.Comparison of functional outcomes after total thyroidectomy and completion thyroidectomy: Hypoparathyroidism and postoperative complications Auris Nasus Larynx. 2019 Feb;46 (1):101-105. doi: 10.1016/j.anl.2018.03.009.

35- Gourin CG, Tufano RP, Forastiere AA, Koch WM, Pawlik TM, Bristow RE. Volume-based trends in thyroid surgery. Arch Otolaryngol Head Neck Surg 2010 doi;136:1191-8.

36- Glockzin G1, Hornung M, Kienle K, Thelen K, Boin M, Schreyer AG, Lighvani HR, Schlitt HJ, Agha A.Completion thyroidectomy: effect of timing on clinical complications and oncologic outcome in patients with differentiated thyroid cancer. World J Surg 2012 doi;36:1168-73.

37- Li YJ, Wang YZ, Yi ZB, Chen LL, Zhou XD. Comparison of completion thyroidectomy and primary total surgery for differentiated thyroid cancer: a meta-analysis. Oncol Res Treat 2015 doi;38:528-31.

38- Calò PG, Pisano G, Piga G, Medas F, Tatti A, Donati M, Nicolosi A Postoperative hematomas after thyroid surgery. Incidence and risk factors in our experience. Ann Ital Chir. 2010 Sep-Oct; doi :81(5):343-7.

39- Duclos A., Peix J.-L., Colin C., Kraimp J.-L, Menegaux F, Pattou, F. . Influence of experience on performance of individual surgeons in thyroid surgery: a prospective cross-sectional multicentre study. BMJ, 2012, doi:10.1136/bmj.d8041

40- Peix JL, Van Box Som P, Olange E, Mancini F, Bourdeix O. Results of reoperations for goiters. Ann Chir 1997 doi; 51 : 3, 217-221.