Incidental parathyroidectomy is a frequent complication of thyroid surgery.

A retrospective study of 3065 patients

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AIM: *The aim of the present study is to investigate the incidence of accidental parathyroidectomy and the connection between the type of surgery, or the resected piece sent for histopathological examination and the number of accidentally excised parathyroid glands.*
MATERIAL AND METHODS: *Patients who had thyroid surgery between January 2005 and December 2014 and were admitted to a surgery clinic from Targu Mures, Romania, were enrolled in this study. For statistical analysis we used Chi-squared test, Student's t-test and ANOVA test, with a p value < 0.05 considered statistically significant.*
RESULTS: *A total of 3065 patients (315 males, 2750 females) were included in our study, with a mean age of 49.66±13.73. The frequence of incidental parathyroidectomy was 15.36%, most patients with IPT (88.95%) had only one parathyroid gland removed and we found a statistically significant association (p = 0.01) between the incidence of IPT and the type of surgery.*
DISCUSSION: *Iatrogenic injury of the parathyroid glands cause hypoparathyroidism which can be transient in majority and permanent in 1.5% of the patients. The most frequent cases with accidental removal of the parathyroid glands were total and subtotal thyroidectomies (79.6%), respectively reinterventions or completion thyroidectomies (10.62%).*
CONCLUSIONS: *Incidental parathyroidectomy is not uncommon following thyroid surgery, even in the hands of experienced surgeons and it is more often seen in female patients with polynodular goiter according to our study. Total thyroidectomies and reinterventions on the thyroid gland increase the risk of incidental parathyroidectomy.*

KEY WORDS: Incidental parathyroidectomy, Hypoparathyroidism, Parathyroid glands

Introduction

A butterfly-shaped organ, the thyroid gland is located in the anterior cervical region where it wraps around the trachea, just inferior to the larynx, at the level of the C5 through T1 vertebrae[1]. It consists of two lobes, the right and the left lobes joined together by a thin structure called the isthmus and some people (about 10-30% of population have a third pyramidal lobe - also known as Lalouette pyramid)[2] arising from the thyroid isthmus, representing the persistent remnant of the thyroglossal duct.

Parathyroid glands (PGs) were first described by Ivar Sandstrom in 1880, but their importance in calcium metabolism was investigated in 1908 by MacCallum and Voegtlin [3].

The location of the upper parathyroid glands is fairly consistent, meanwhile the lower PGs are more frequently ectopic and with wider distribution [4]. Supernumerary PGs are discovered in about 2–6% of patients, and fewer than four PGs are reported in 3% of cases [5].

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ABREVIATIONS

IPT = incidental parathyroidectomy
PGs = parathyroid glands
RLN = recurrent laryngeal nerve
PTH = parathyroid hormone

Iatrogenic injury of the parathyroid glands is a common complication following total thyroidectomy causing hypoparathyroidism which can be transient in majority and permanent in 1.5% of the patients [6]. This can lead to hypocalcemia because parathyroid hormone (PTH) secretion is impaired and cannot mobilize calcium from bone, reabsorb calcium from the distal nephron or stimulate renal 1α-hydroxylase activity [7]. Since thyroid surgeons know that potential risk, many patients are empirically treated with calcium to avoid symptoms of hypocalcemia, and this can mask who truly has transient hypoparathyroidism and who does not.

Material And Method

A retrospective study was conducted during January 2005 and December 2014 in four surgery clinics from Targu Mures, Romania. This study included 3065 patients with thyroid gland surgery. Following clinical data collection, gender, age, surgical procedure, pathologic findings, number of incidentally removed parathyroid glands, TNM stage were registered. All patients obtained written informed consent. Inclusion criteria targeted patients who have undergone thyroid surgery regardless of age or sex. Exclusion criteria targeted cases where a deliberate parathyroidectomy was performed or those in which the parathyroid glands were located intrathyroidal, and their excision could not be avoided. Patients' data was processed using a Microsoft Office Excel database. For statistical assessment, Microsoft Office Excel software was used for creating specific data sheets. Data analysis was performed using Graph Pad Prism 7 and SPSS 20.0 softwares. For statistical analysis we used Chi-squared test, Student's t-test and ANOVA test. A p value < 0.05 was considered statistically significant, with 95% confidence interval.
Within this study, besides patients' demographic data, we investigated the incidence of accidental parathyroidectomy and the number of injured parathyroid glands during surgeries. We also analyzed the connection between the type of surgery, or the resected piece sent for histopathological examination and the number of accidentally excised parathyroid glands and correlated the histopathological diagnosis with the incidence of incidental parathyroidectomy.

Results

During the study period, a total of 3065 patients (315 males, 2750 females) underwent thyroid surgery in our hospitals, with a mean age of 49.66 ± 13.73.
Histopathological examination of the resected specimen revealed benign disease and malignancy in 2212 (72.1%) and 725 (23.7%) cases, respectively 128 (4.2%) patients had normal thyroid tissue removed. Analyzing the histopathological results, the most common benign diagnosis was polynodular goiter (68.2%) and thyroid adenoma (15.5%) and among malignant pathology, papillary thyroid carcinoma was the most common - 52.8%. (Table I)
Regarding the type of surgery, most patients benefited from total or near-total thyroidectomy (75.7%) and only in 12.3% of cases lobectomy was performed with or

TABLE I - *Demographic and pathological characteristics. Period of study: January 2005 – December 2014Patients: 3065*

	Number	Percentage
Sex		
Male	315	10.3%
Female	2750	89.7%
Age	49.66 ± 13.73	Range 1-98 years
Thyroid pathology		
Benign	2212	72.1%
Malignant	725	23.7%
Normal tissue	128	4.2%
Benign diagnosis		
Multinodular goiter	1509	68.2%
Basedow Graves	148	6.7%
Thyroiditis	100	4.5%
Follicular adenoma	343	15.5%
Others (thyroid nodules)	112	5.1%
Malignant diagnosis		
Papillary thyroid cancer	383	52.8%
Follicular carcinoma	5	0.7%
Myeloid thyroid cancer	19	2.6%
Anaplastic thyroid cancer	16	2.2%
Metastases	9	1.2%
Microcarcinomas	276	38.2%
Others	17	2.3%
Type of surgery		
Total/Near-total thyroidectomy	2320	75.7%
Lobectomy	377	12.3%
Reintervention	295	9.6%
Radical dissection of the neck	73	2.4%

TABLE II - *Incidental parathyroidectomy.*

Incidental parathyroidectomy	15.36% (471 patients)
Number of removed PGs	
1	88.95%
2	10.19%
3	0.86%

without isthmus resection. 9.6% of patients underwent a complementary thyroidectomy, thus being a reintervention and in 2.4% of cases a radical dissection of the neck was performed (Table I).

The cases were divided into two groups after analyzing the histopathological results, the first group included patients with thyroid gland surgery who had incidental parathyroidectomy (IPT) during the operation and the second group comprised cases without incidental parathyroidectomy.

In our study the incidence of accidental parathyroidectomy was 15.36%; 471 patients had between 1 and 3 removed parathyroid glands. In most patients with IPT (88.95%), only one PG was removed. However, 10.19% and 0.86% patients had two or three PGs removed, respectively. The univariate analysis did not identify age as risk factor for IPT (Table II).

We looked for the existence of a statistically significant association between the type of surgery, respectively the resected piece sent for histopathological examination and the number of accidentally excised parathyroid glands. The most common situations in which the parathyroid glands were removed were those with removal of both thyroid lobes, while a protective factor for PGs turned out to be removal of a small, well-specified operative piece, such as a thyroid nodule. With a p = 0.04, we deduce that the extension of the surgery increases the risk of accidental parathyroidectomy.

Our study showed a statistically significant association (p = 0.01) between the incidence of IPT and the type of surgery. In case of total or subtotal thyroidectomy and reinterventions on the thyroid gland, were described significantly more cases with IPT (79.6%), while in isthmlobectomies, the incidence of accidental removal of parathyroids was only 8.3% (Table III).

We correlated the histopathological diagnosis with the incidence of IPT.

In 74.5% of the cases that had this complication the diagnosis was polynodular goiter and in only 2.1% of the cases it was a thyroid nodule, statistically significant difference (p = 0.02), giving thyroid nodule diagnosis the role of a protective factor (Table III).

Discussion

Incidental parathyroidectomy is not uncommon following thyroid surgery, even in the hands of experienced surgeons. The variability in location, number, size, and shape of parathyroid glands make them vulnerable to iatrogenic trauma. The incidence of IPT in our study was 15.36%, which falls within the rates reported in the international literature, between 5.2 and 21.6% [8]. By developing a thorough understanding of thyroid anatomy and with a careful dissection and good exposure of anatomical structures, the surgeon can minimize each patient's risk of complications post thyroidectomy. In our study, 88.95% of cases with IPT, a single parathyroid was removed, a percentage that is similar to that reported in the literature (67.6% - 86%). However, we have a significant percentage of cases where two parathyroid glands were removed (10.19%) and three (0.84%), respectively [9,10].

There is still being discussed how many PGs should be found during thyroidectomy to prevent hypoparathyroidism, or if the surgeon should or shouldn't actively

Table III - *Comparison of incidental parathyroidectomy (IPT) and nonincidental parathyroidectomy (non-IPT) groups.*

N	IPT group 471	Non-IPT group 2594	P value
Age (years)	49.67 ± 13.37	49.66 ± 13.79	0.98
Sex			
Male	37 (11.7%)	278 (88.3%)	0.04
Female	434 (92.1%)	2316 (7.9%)	
Surgical intervention			
Total / Near-total thyroidectomy	375 (79.6%)	1945 (74.98%)	0.01
Isthmlobectomies	39 (8.3%)	338 (13.03%)	
Reinterventions	50 (10.62%)	245 (9.44%)	
Neck dissection	7 (1.48%)	66 (2.55%)	
Histopathologic diagnosis			
Benign	376 (79.8%)	1836 (70.8%)	0.001
Malignant	70 (14.9%)	655 (25.2%)	
Normal thyroid tissue	25 (5.3%)	103 (4%)	
Benign diagnosis			
Multinodular goiter	280 (74.5%)	1223 (66.61%)	0.02
Basedow Graves	21 (5.58)	126 (6.86%)	
Thyroiditis	25 (6.64%)	110 (6.1%)	
Follicular adenoma	42 (11.18%)	300 (16.33%)	
Others (thyroid nodules)	8 (2.1%)	70 (3.82%)	

dissect and identify all the PG's. Most recent studies suggest that at least three PGs should be preserved in order to avoid permanent hypoparathyroidism [9,10,11] and the number of parathyroid glands left in situ is an important factor that influences postoperative hypocalcemia [12]. According to several studies, the extent of resection has an important role in postoperative hypoparathyroidism [13,14]. Testini et al. and Dubernard et al. showed that total thyroidectomy with central neck dissection or completion thyroidectomy are associated more frequently with postoperative complications such as hypoparathyroidism [15,16]. Similar findings were obtained in our study. The most frequent cases with accidental removal of the parathyroid glands were total and subtotal thyroidectomies (79.6%), respectively reinterventions or completion thyroidectomies (10.62%). Patients with total removal of thyroid lobes had a significantly higher risk of IPT (p=0.01) than those where just a lobectomy was done.

In subtotal thyroidectomy, the risk of hypoparathyroidism is lower than in total thyroidectomy where the entire tissue of the thyroid gland is removed. In a study [17] published in 2021 involving 285 patients was showed that a prolonged operative time, a low PTH level on day one postoperative and high weight of thyroid gland are strong risk factor of permanent hypoparathyroidism post-thyroidectomy. Also, in another study including 933 patients in a center from Ankara,Turkey was demonstrated a significant association between elderly patients or high volume of thyroid gland and post-operative hypoparathyroidism [18].

There was no statistically significant difference between the two groups (with IPT and non-IPT) regarding the age (p=0.98) or the presence of thyroiditis (p=0.94), similar results as in other studies [10].

Hypoparathyroidism is considered as one of the mostly commonly seen complications in thyroid surgery. Thus, surgical procedures like total thyroidectomy require special skills and surgical training to reduce complications associated with it. We believe that such interventions, if are performed by experienced surgeons and eventually using optical magnification leads to significantly smaller risk of postoperative complications such as hypoparathyroidism and RLN lesions, as confirmed by other studies from the literature [16,19,20,21].

Limitations of our study include its retrospective nature and the fact that it is a study conducted in only one city from Romania.

Conclusion

Incidental parathyroidectomy is not an uncommon complication following thyroid surgery, and it is more often seen in female patients with polynodular goiter according to our study. Total thyroidectomies and reinterventions on the thyroid gland increase the risk of incidental parathyroidectomy. Age and the presence or absence of thyroiditis do not represent factors which could significantly influence the possibility of incidental parathyroidectomy. Even an experienced thyroid surgeon is not always able to identify all four PGs during thyroidectomy, however, preserving the PGs is the key to minimize postoperative hypoparathyroidism.

Riassunto

OBIETTIVO: Lo scopo del presente studio è di indagare l'incidenza della paratiroidectomia accidentale e la connessione tra il tipo di intervento chirurgico, o il pezzo asportato inviato per l'esame istopatologico e il numero di ghiandole paratiroidi asportate accidentalmente.

MATERIALE E METODI: Questo studio ha incluso 3065 pazienti che hanno subito un intervento chirurgico alla tiroide tra gennaio 2005 e dicembre 2014 e sono stati ricoverati in una delle quattro cliniche chirurgiche di Targu Mures, Romania. Dopo la raccolta dei dati clinici, sono stati registrati sesso, età, procedura chirurgica, reperti patologici, numero di ghiandole paratiroidi rimosse accidentalmente, stadio TNM. I criteri di esclusione riguardavano i casi in cui era stata eseguita una paratiroidectomia deliberata o quelli in cui le ghiandole paratiroidi erano localizzate intratiroidee e la loro escissione non poteva essere evitata. L'analisi dei dati è stata eseguita utilizzando il software Graph Pad Prism 7 e SPSS 20.0 e per l'analisi statistica abbiamo utilizzato il test chi quadrato, il test T-Student e il test ANOVA, con un valore p <0.05 considerato statisticamente significativo, con un intervallo di confidenza del 95%.

RISULTATI: Un totale di 3065 pazienti (315 maschi, 2750 femmine) sono stati inclusi nel nostro studio, con un'età media di 49.66 ± 13.73. Analizzando i risultati istopatologici, la diagnosi benigna più comune era il gozzo polinodulare (68.2%) e l'adenoma tiroideo (15.5%) e tra le patologie maligne, il carcinoma papillare della tiroide era il più comune – 52.8%. Per quanto riguarda il tipo di intervento chirurgico, la maggior parte dei pazienti hanno beneficiato di tiroidectomia totale o quasi totale (75.7%) e solo nel 12.3% dei casi la lobectomia è stata eseguita con o senza resezione dell'istmo. La frequenza della paratiroidectomia accidentale nel nostro studio era del 15.36%, la maggior parte dei pazienti con IPT (88.95%) aveva solo una ghiandola paratiroidea rimossa e il nostro studio ha mostrato un'associazione statisticamente significativa (p = 0.01) tra l'incidenza di IPT e il tipo di intervento chirurgico, ma non vi era alcuna differenza statisticamente significativa tra i due gruppi (con IPT e non IPT) per quanto riguarda l'età (p=0.98) o la presenza di tiroidite (p=0.94). Le situazioni più comuni in cui sono state rimosse le ghiandole paratiroidi sono state quelle con rimozione di entrambi i lobi tiroidei, mentre un fattore protettivo per i PG si è rivelato essere la rimozione di un piccolo pezzo operatorio

ben specificato, come un nodulo tiroideo (p = 0.04).
Discussione: La variabilità nella posizione, numero, dimensione e forma delle ghiandole paratiroidi le rende vulnerabili al trauma iatrogeno. Il danno iatrogeno delle ghiandole paratiroidi causa ipoparatiroidismo che può essere transitorio nella maggioranza e permanente nell'1.5% dei pazienti. L'incidenza dell'IPT nel nostro studio è stata 15.36%, che rientra nei raporti della letteratura internazionale, tra il 5.2 e il 21.6%. I casi più frequenti di rimozione accidentale delle paratiroidi sono stati tiroidectomie totali e subtotali (79.6%), rispettivamente reinterventi o tiroidectomie di completamento (10.62%). Nel nostro studio, nell' 88.95% dei casi con IPT è stata rimossa una singola paratiroide, una percentuale simile a quella riportata in letteratura (67.6% - 86%). L'ipoparatiroidismo è considerato una delle complicanze più comunemente osservate nella chirurgia tiroidea. Pertanto, procedure chirurgiche come la tiroidectomia totale richiedono abilità speciali e formazione chirurgica per ridurre le complicanze ad essa associate.
Conclusioni: La paratiroidectomia accidentale non è rara dopo un intervento chirurgico alla tiroide, anche nelle mani di chirurghi esperti e secondo il nostro studio è più frequente nelle pazienti di sesso femminile con gozzo multinodulare. La tiroidectomia totale e i reinterventi sulla tiroide aumentano il rischio di paratiroidectomia accidentale. L'età e la presenza o assenza di tiroidite non rappresentano fattori che potrebbero influenzare significativamente la possibilità di una paratiroidectomia accidentale.

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