World J. Surg. 22, 718–724, 1998

WORLD
Journal of
SURGERY

Hypocalcemia following Thyroid Surgery: Incidence and Prediction of Outcome

François Pattou, M.D.,[1] Frederic Combemale, M.D.,[1] Sylvain Fabre, M.D.,[1] Bruno Carnaille, M.D.,[1]
Marc Decoulx, M.D.,[2] Jean-Louis Wemeau, M.D.,[2] Alain Racadot, Ph.D.,[3] Charles Proye, M.D.[1]

[1]Department of General and Endocrine Surgery, Clinique Chirurgicale Adulte Est Hôpital Huriez, Centre Hospitalier et Universitaire de Lille, 1 Place de Verdun, 59037 Lille, France
[2]Department of Endocrinology, Clinique Chirurgicale Adulte Est Hôpital Huriez, Centre Hospitalier et Universitaire de Lille, 1 Place de Verdun, 59037 Lille, France
[3]Laboratory of Biochemistry, Clinique Chirurgicale Adulte Est Hôpital Huriez, Centre Hospitalier et Universitaire de Lille, 1 Place de Verdun, 59037 Lille, France

Abstract. Postoperative hypocalcemia is a common and most often transient event after extensive thyroid surgery. It may reveal iatrogenic injury to the parathyroid glands and permanent hypoparathyroidism. We prospectively evaluated the incidence of hypocalcemia and permanent hypoparathyroidism following total or subtotal thyroidectomy in 1071 consecutive patients operated during 1990–1991. We then determined in a cross-sectional study which early clinical and biochemical characteristics of patients experiencing postoperative hypocalcemia correlated with the long-term outcome. Postoperative calcemia under 2 mmol/L was observed in 58 patients (5.4%). In 40 patients hypocalcemia was considered severe (confirmed for more than 2 days, symptomatic or both). At 1 year after surgery five patients (0.5%) had persistent hypocalcemia. We found that patients carried a high risk for permanent hypoparathyroidism if fewer than three parathyroid glands were preserved in situ during surgery or the early serum parathyroid hormone level was ≤ 12 pg/ml, the delayed serum calcium levels ≤ 8 mg/dl, or the delayed serum phosphorus level ≥ 4 mg/dl under oral calcium therapy. When one or more of these criteria are present, long-term follow-up should be enforced to check for chronic hypocalcemia and to avoid its severe complications by appropriate supplement therapy.

A postoperative decrease of serum calcium is frequently observed within 2 to 5 days after a total or subtotal thyroidectomy, requiring exogenous replacement therapy to alleviate clinical symptoms. In several series [1–12], the incidence of hypocalcemia varied from 1.6% to more than 50%. Among the potential factors causing this decrease of serum calcium, hemodilution [13], calcitonin release [14], and "hungry bone syndrome" were implicated in patients with hyperthyroidism and osteodystrophy [15]. In patients experiencing significant hypocalcemia, the most probable cause is certainly hypoparathyroidism secondary to trauma, devascularization, or inadvertent excision of one or more parathyroid gland(s) during surgery. In most cases serum calcium levels normalize within a few months, with the spontaneous recovery of parathyroid function. In a few patients however, hypoparathyroidism persists after 1 year and must be considered permanent. This dire complication represents a major concern for thyroid surgeons as the consequences of chronic hypocalcemia are often insidious and potentially severe [16]. Permanent hypocalcemia is a common cause of malpractice litigation after endocrine surgery. The risk of permanent hypoparathyroidism following thyroidectomy remains unclear, varying among recent series from zero up to 10% [1–12]. Moreover, the risk of permanent hypoparathyroidism is poorly correlated with early serum calcium levels in patients experiencing hypocalcemia following thyroid surgery. Clinically relevant predictive factors associated with the long-term recovery of normal parathyroid function are lacking.

In this study we prospectively evaluated the incidence of hypocalcemia and permanent hypoparathyroidism following thyroidectomy in a department of endocrine surgery where a large volume of thyroid surgery cases are treated. We also sought to determine in a cross-sectional study which early clinical and biochemical characteristics of patients experiencing postoperative hypocalcemia correlated with the long-term outcome.

Materials and Methods

Longitudinal Study

This prospective study was designed to evaluate the incidence of postoperative hypocalcemia and permanent hypoparathyroidism after total or subtotal thyroidectomy. All patients who were operated on in the Department of General and Endocrine Surgery at University Hospital of Lille from January 1990 to December 1991 were included. The fasting serum calcium and serum phosphorus levels were measured daily before and after surgery until the day of hospital discharge, which was usually on the second postoperative day. Hypocalcemia was defined as a serum calcium level under 8.0 mg/dl (2 mmol/L) on at least two consecutive measurements. When the serum calcium remained under 8.0 mg/dl for more than 2 days, or when patients experienced clinical symptoms and signs of hypocalcemia (paresthesia

This International Association of Endocrine Surgeons (IAES) article was presented at the 37th World Congress of Surgery International Surgical Week (ISW97), Acapulco, Mexico, August 24–30, 1997.
Correspondence to: C. Proye, M.D.

or positive Chvostek's sign), hypocalcemia was considered severe and 1-84 parathyroid hormone (PTH) measurement was performed before starting intravenous or oral calcium supplementation. After the relief of clinical symptoms for a 24-hour period, patients were deemed ready for hospital discharge with a prescription of an oral calcium substitute (3 g/day).

After discharge, and within 1 to 3 weeks on calcium supplementation, all patients who experienced severe postoperative hypocalcemia were evaluated in the outpatient clinic to control serum calcium and serum phosphorus levels and to titrate the substitution therapy. All patients were thereafter seen at least once every 3 months in our department or by the referring physician. They were followed until normalization of their serum calcium after withdrawal of any substitutive therapy with calcium or vitamin D for more than 1 week. Permanent hypoparathyroidism was defined by the requirement for vitamin D or calcium supplementation (or both) to maintain eucalcemia 1 year after thyroidectomy.

Cross-sectional Study

We performed a retrospective cross-sectional study to analyze the risk factors for permanent hypoparathyroidism in patients experiencing severe postoperative hypocalcemia. We compared the clinical and biochemical characteristics of the patients who spontaneously recovered normal parathyroid function with those of a group of patients in whom hypoparathyroidism was found to be permanent. To allow statistical comparison, seven patients operated on during 1992–1996 who were found to have permanent hypoparathyroidism and for whom early information was available were also included in this cross-sectional study.

All patients were examined for the type of thyroid disease, previous neck surgery, and parathyroid preservation during surgery, with or without autotransplantation. We also examined serum calcium and serum phosphorus levels before surgery and before starting calcium supplementation on the second to the fifth postoperative day. Likewise, early serum PTH was determined, as were the delayed serum calcium and serum phosphorus levels during the first outpatient visit 1 to 3 weeks after discharge.

Operative Technique

All operations were performed by staff surgeons or senior registrars (chef de clinique) and consisted of a subtotal or total thyroidectomy. In all patients, every effort was made to identify and preserve the recurrent laryngeal nerves and the four parathyroid glands. For benign thyroid disease, total thyroid resection was conducted intracapsularly when necessary to preserve the vascularization of the superior parathyroid glands (near-total thyroidectomy). When vascularization of a parathyroid gland appeared compromised, it was selectively resected and autotransplanted in the homolateral sternocleidomastoid muscle.

Biochemical Assays

Serum levels of PTH 1-84 were measured with an immunoradiometric assay (N-tact PTH SP Kit; Incstar, Stillwater, OK, USA). Normal values of serum PTH with this technique are 10 and 55 pg/ml, and the minimal level of PTH detected is 5 pg/ml. Serum calcium and serum inorganic phosphorus levels were routinely measured with an automated colorimetric method (Randox Laboratories, Crumlin, UK). Normal values in our hospital are 8.1 to 10.4 mg/dl (2.02–2.60 mmol/L) for serum calcium and 2.68 to 4.5 mg/dl (0.87–1.45 mmol/L) for serum phosphorus.

Table 1. Incidence of postoperative hypocalcemia and permanent hypoparathyroidism after total or subtotal thyroidectomy in 1071 consecutive patients.

Parameter	Postoperative hypocalcemia	Severe postoperative hypocalcemia	Permanent hypoparathyroidism
No. patients	58	40	5
Incidence (%)	5.4	3.7	0.5

Statistical Analysis

All results were expressed as the mean ± standard error of the mean (SEM). The evolution of serum calcium and serum phosphorus during the hospital stay of both groups of patients was compared using ANOVA and the Student's *t*-test for repeated measures. The univariate relation between outcome of hypocalcemia and patient characteristics was examined with Fischer's exact test for categoric variables and the Mann-Whitney test for continuous variables. Differences were considered significant when $p < 0.05$. All analyses were performed with a statistic software package (Stat-View, Abacus Concept, Berkeley, CA, USA).

Results

Longitudinal Study

Within the 2-year period of the study, 1071 patients were operated on in our department by total or subtotal thyroidectomy. Among them, 58 experienced postoperative hypocalcemia, of whom 40 were considered to have severe hypocalcemia. All patients were followed up, and 53 of them (91%) became normocalcemic within 1 week to 6 months. Five patients (9%), all with initially severe postoperative hypocalcemia, still required calcium substitution or vitamin D therapy (or both) 1 year after thyroidectomy. Hypoparathyroidism was confirmed in these five patients (10 and 13 pg/ml in two and undetectable serum PTH levels in three) and was considered permanent. The incidence of postoperative hypocalcemia and permanent hypoparathyroidism after thyroidectomy is summarized in Table 1.

Cross-sectional Study

The clinical and biochemical characteristics of the 12 patients with permanent hypoparathyroidism included in the study are detailed in Table 2. All of the individual values were available for the univariate analysis, except the number of preserved parathyroid glands and the delayed serum calcium and phosphorus levels for, respectively, two and five patients with transient hypocalcemia. No differences were observed between the initial evolution of serum calcium and serum phosphorus levels of patients with permanent hypoparathyroidism and those of the 35 consecutive patients from the longitudinal study who experienced severe postoperative hypocalcemia and spontaneously recovered (Fig. 1).

Table 2. Individual clinical and biochemical characteristics of 12 patients with permanent hypoparathyroidism after thyroidectomy.

Patient[a]	Diagnosis	Previous neck surgery	No. of preserved parathyroid glands			Calcium (mg/dl)		Phosphorus (mg/dl)		Serum PTH (pg/ml)	
			In situ	Transplanted	Total	Postop. nadir	Delayed	Max. postop.	Delayed	Early postop.	At 1 year
1	Multinodular goiter	Yes	0	0	0	73	79	37	43	UD	UD
2	Grave's disease	No	2	2	4	59	82	68	50	UD	UD
3	Carcinoma	No	2	0	2	73	64	58	41	8	UD
4	Carcinoma	No	2	2	4	72	93	48	40	11	10
5	Carcinoma	Yes	1	0	1	63	81	63	45	10	13
6	Carcinoma	No	3	0	3	71	73	56	51	11	11
7	Multinodular goiter	No	2	0	2	70	70	56	46	12	9
8	Multinodular goiter	No	1	1	2	75	81	52	45	12	11
9	Toxic goiter	No	2	0	2	64	69	45	39	11	10
10	Toxic goiter	No	2	1	3	65	60	37	64	10	14
11	Recurrent goiter	Yes	2	0	2	66	96	55	40	UD	UD
12	Grave's disease	No	1	1	2	65	55	34	82	UD	UD

UD: undetectable.
[a]Patients 1 to 5 were included in the longitudinal study.

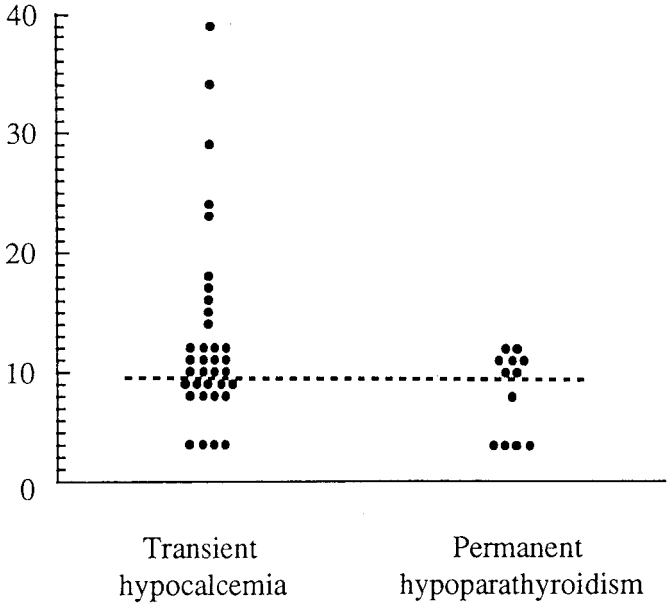

Fig. 1. Early serum parathyroid hormone level (picograms per milliliter) in 35 patients with transient postoperative hypocalcemia and 12 patients with permanent hypoparathyroidism. Bottom line represents the low normal value.

Table 3. Univariate relation between clinical and biochemical characteristics of patients and outcome of postoperative hypocalcemia.

Patient characteristics	Transient postoperative hypocalcemia (n = 35)	Permanent hypocalcemia (n = 12)	p*
Diagnosis			
Hyperthyroidism	5 (14%)	4 (33%)	0.21
Carcinoma	8 (23%)	4 (33%)	0.47
Surgery			
Reoperation	2 (6%)	3 (25%)	0.09
Preserved parathyroid glands (no.)	3.3 ± 0.2	2.2 ± 0.3	<0.01
In situ	2.7 ± 0.2	1.7 ± 0.2	<0.01
Autotransplanted	0.6 ± 0.1	0.6 ± 0.2	0.94
During hospital stay			
Serum calcium nadir (mg/dl)	6.9 ± 0.1	6.8 ± 0.1	0.84
Maximal serum phosphorus (mg/dl)	5.1 ± 0.2	5.1 ± 0.3	0.97
Early postoperative PTH (pg/ml)	12.6 ± 1.5	7.1 ± 1.5	0.11
One week after treatment			
Serum calcium (mg/dl)	8.6 ± 0.1	75 ± 0.4	<0.01
Serum phosphorus (mg/dl)	3.7 ± 0.2	49 ± 0.4	<0.01

Results are given as the number or the mean ± SEM.
*Univariate analysis using the Fisher's exact test for categoric variables and the Mann-Whitney U-test for continuous variables.

The results of the comparison of the clinical and biochemical characteristics of the two groups of patients are summarized in Table 3. Although hyperthyroidism, carcinoma, and previous neck surgery were more frequent in the patients with permanent hypoparathyroidism, this difference did not appear to be statistically significant ($p > 0.05$). The number of parathyroid glands preserved in situ during surgery was highly correlated with the outcome of the hypocalcemia ($p = 0.01$). As shown in Figure 1, the initial evolution of serum calcium and phosphorus levels, as well as the mean calcium nadir and maximal phosphorus (Table 3), were identical in the two groups. The mean serum PTH levels of both groups of patients were not significantly different, with individual figures represented in Figure 2. Delayed serum calcium and serum phosphorus measured 1 week after the initiation of calcium substitution, were highly correlated with the long-term outcome ($p = 0.003$ and $p < 0.0001$ respectively). Overall, four clinically relevant criteria were found to be significantly correlated with the spontaneous recovery from postoperative hypocalcemia (Table 4).

Discussion

Postoperative hypocalcemia is a major concern following thyroid surgery. It often extends the duration of the hospital stay and the need for biochemical tests, and it significantly increases the overall cost of a thyroidectomy. When severe, it can lead to

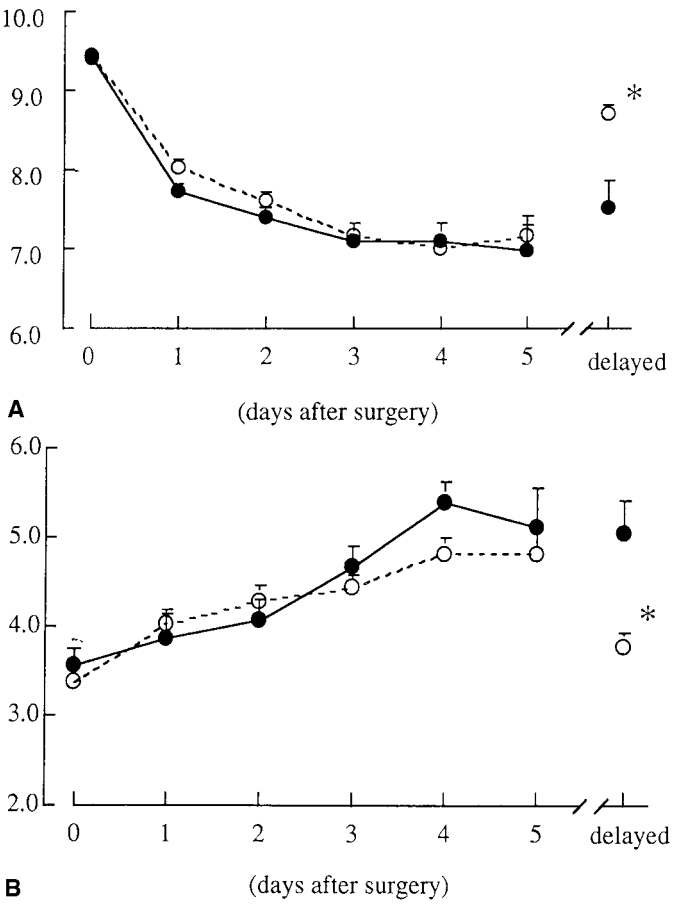

Fig. 2. Serum calcium **(A)** and serum phosphorus **(B)** levels (nanograms per deciliter) following thyroidectomy in 35 patients with transient postoperative hypocalcemia (open circles) and 12 patients with permanent hypoparathyroidism (closed circles). No difference was observed during the first 5 days after surgery. After 1 to 3 weeks on calcium supplementation (delayed), patients with permanent hypoparathyroidism had significantly lower serum calcium levels and significantly higher levels of serum phosphorus than the patients with transient postoperative hypocalcemia (*$p < 0.01$, Mann-Whitney test).

Table 4. Clinically relevant criteria correlated with the outcome of patients experiencing severe postoperative hypocalcemia.

Criterion	p*
No. of parathyroid glands preserved in situ ≥ 3	0.02
Postoperative PTH $>$ 12 pg/ml	0.04
Delayed serum Ca $>$ 8.0 mg/dl	0.005
Delayed serum P $<$ 4.0 mg/dl	$<$ 0.001

*Univariate analysis using Fisher's exact test.

serious complications and require intravenous therapy to alleviate the clinical symptoms [17]. Although hypocalcemia reverses spontaneously in most cases, it can remain permanent when caused by irreversible injury to the parathyroid glands. Lifelong therapy and follow-up are then mandatory to avoid the subtle but severe and potentially lethal complications of chronic hypocalcemia [16]. In this prospective survey, postoperative hypocalcemia was observed in 5.7% of 1071 patients undergoing total or subtotal thyroidectomy. Permanent hypoparathyroidism was found in five patients (0.5%). These figures, consistent with previous reports from our department [8, 18], compare favorably with most of the results reported in the literature (Table 5).

Table 5. Incidence of postoperative hypocalcemia and permanent hypoparathyroidism following thyroid surgery reported in the literature.

Study	Year	Patients at risk (no.)	Postoperative hypocalcemia (%)	Permanent hypoparathyroidism (%)
Jacobs et al. [1]	1983	213	27.7	2.8
Pederson et al. [2]	1984	105	21.9	8.6
Schwartz & Friedman [3]	1987	183	17.5	3.3
Peix & Zabot [4]	1988	171	3.5	0.0
Deard et al. [5]	1988	223	33.6	5.4
Kraimps et al. [6]	1988	102	16.7	2.0
Tovi et al. [7]	1989	100	9.0	4.0
Prades et al. [8]	1990	118	22.0	9.3
Proye et al. [9]	1990	477	5.9	0.2
Megherbi et al. [10]	1992	354	9.9	2.3
Olson et al. [11]	1996	194	53.6	0.5
Al-Suliman et al. [12]	1997	935	1.6	0.9

Following thyroid surgery, postoperative hypocalcemia is reported to occur in a few to more than 50% of patients. Various factors account for these differences in the literature, such as the definition of hypocalcemia, the type of thyroid disease, and the surgical technique for thyroidectomy. To focus our study on clinically significant hypocalcemia, we considered as hypocalcemic only patients with a serum calcium level under 8 mg/dl on two occasions and who in most cases required calcium substitution. Our study group reflects the referral pattern of our department during two consecutive years and included patients with hyperthyroidism or thyroid carcinoma, generally considered at risk for hypocalcemia following thyroidectomy [19]. Despite potentially excellent long-term results, the liberal resection and autotransplantation of the parathyroid glands carries a high risk of temporary but clinically significant hypocalcemia [11]. Our policy for thyroidectomy calls for preservation of the parathyroid glands in situ and their vascularization. The blood supply to the upper glands arises from the inferior thyroid artery and from anastomoses with the superior thyroid artery [20]. When deemed necessary for the preservation of these anastomosing branches, we prefer to conduct the dissection intra-capsularly and to perform a "near-total" thyroidectomy.

In addition to injury to the parathyroid glands during surgery, various factors may contribute to the decreased serum calcium following thyroidectomy. As shown in Figure 2, the early serum PTH levels remained detectable in more than half of the patients experiencing severe hypocalcemia. It was above 12 pg/ml in 10

patients, who all recovered spontaneously. In five patients, including three with hyperthyroidism, parathyroid function appeared to be correlated with the serum calcium levels, with the serum PTH ranging from 23 to 39 pg/ml.

Various factors may account for the decrease in serum calcium levels in these patients. Following thyroidectomy, whether unilateral or bilateral, moderate, asymptomatic hypocalcemia is observed within 12 hours following surgery, and it recovers spontaneously by 24 hours in most patients. Simultaneously, serum phosphorus slightly decreases at 24 hours [13, 21]. Hemodilution during the perioperative period may be responsible for these changes and explains their occurrence with other extracervical operations of the same magnitude and duration as with thyroidectomy [13]. Elevation of serum calcitonin secondary to manipulation of the thyroid was also initially suspected to participate in this calcium decrease [14] but was not confirmed in recent studies [13, 19, 21, 22]. In patients with hyperthyroidism, the postoperative reversal of osteodystrophy and the accretion of calcium in bones may also contribute to the decreased serum calcium.

When normal parathyroid function can be documented, this "hungry bone syndrome" appears to be the most probable cause of hypocalcemia [23]. In this case the serum calcium generally achieves its nadir within 48 hours after surgery. The risk of hypocalcemia is not alleviated by the correction of hyperthyroidism within a few weeks before thyroidectomy [24]. It is correlated with the pretreatment serum levels of free thyroxine [19] and with markers of the bone turnover rate, such as serum alkaline phosphatase levels [13] and urinary hydroxyproline [24].

Although these mechanisms may have contributed to a further decrease in serum calcium levels, they hardly explain the frank, prolonged hypocalcemia observed in our patients. In most of the cases, the serum calcium nadir was delayed to the third or fourth day, a feature frequently observed after total parathyroid gland ablation during major neck surgery. Even when detectable, the serum PTH was obviously inappropriate ($\leq$ 12 pg/ml) compared to the serum calcium level in 75% of the patients. In these patients, postoperative hypoparathyroidism appeared to be the major determinant of the occurrence of clinically relevant hypocalcemia following thyroid surgery. Various mechanisms can impair parathyroid function during thyroid surgery, including trauma to, devascularization of, or inadvertent excision of the parathyroid glands. In light of the terrible consequences of permanent hypoparathyroidism, the major concern when facing thyroidectomy-induced hypocalcemia is the potential for spontaneous recovery of parathyroid function. Although highly desirable, reliable early predictive criteria remain to be described.

We found no significant correlation between the preoperative clinical characteristics of the patients and the long-term outcome of their hypocalcemia. Permanent hypoparathyroidism is slightly more frequent in cases of thyroidectomy for hyperthyroidism, thyroid carcinoma, or after previous neck surgery—three conditions in which parathyroid preservation may be jeopardized by technical difficulties. Indeed, the number of parathyroid glands preserved during thyroidectomy appeared to be the major determinant of the outcome. When three or more parathyroid glands could be identified and preserved in situ at surgery, spontaneous recovery was observed in all cases but one (positive predictive value 95%). As already described by others [25], the safety of parathyroid autotransplantation was not absolute in our experience. Permanent hypoparathyroidism occurred in two patients despite the preservation in situ of two glands and autotransplantation of the two others. These findings seem in contradiction with other reports [11] and may be related to differences in the transplantation technique.

The physical preservation of parathyroid tissue is a prerequisite but does not assume recovery of its function in all cases. In contrast to Hans and Tai Lee [26], we found that the evolution of serum calcium and serum phosphorus levels within the first few days following surgery, before calcium substitution, was identical in both groups of patients and of little predictive value for the outcome. Early assessment of parathyroid function appeared to be a useful tool, as serum PTH levels above 12 pg/ml were always associated with a spontaneous recovery. On the other hand, use of the negative predictive value of this test remained limited. Even when poor early parathyroid function could be documented, hypocalcemia recovered spontaneously within a few months in 90% of cases. In four patients with transient hypocalcemia, no serum PTH could be detected during the early period following thyroidectomy. After experimental devascularization of parathyroid tissue, an immediate decrease in PTH secretion is observed as is the complete vanishing of blood vessels within 2 to 4 days, associated with a central ischemic necrosis. De novo and peripheral microvascularization is observed after 1 week followed by detection of PTH secretion. The graft is not completely revascularized before 3 weeks [27]. These findings are corroborated by the spontaneous normalization of the serum calcium level within 6 weeks in patients undergoing deliberate autotransplantation of parathyroid glands [11]. One cannot exclude the progressively increased function of a supernumerary, rudimentary fifth parathyroid gland at a thymic or mediastinal site. In our experience, such a gland is found in 13% of embryos upon necropsy and is encountered in 30% of hemodialysis patients who undergo parathyroidectomy. Conversely, hypocalcemia may remain despite the persistence of slight secretion of PTH, as observed in 66% of our patients with permanent hypoparathyroidism. This finding exemplifies the limited proliferative capacity of normal parathyroid cells and the need to preserve a sufficient mass of parathyroid tissue at surgery.

An interesting finding was the high predictive value of serum calcium and serum phosphorus levels when patients had already received calcium supplementation but no vitamin D. As early as 1 week after discharge, the consequences of ongoing recovery of parathyroid function on calcium and phosphorus homeostasis could already be seen in most patients who subsequently recovered. Conversely, when serum calcium remained at 8 mg/dl or below or the serum phosphorus levels were 4 mg/dl or above (or both), we found that the risk for permanent hypoparathyroidism was as high as 66% and 69%, respectively. Eventually, all patients with both delayed serum calcium levels above 8 mg/dl and serum phosphorus levels below 4 mg/dl spontaneously recovered normal parathyroid function. This simple test appeared to be of value to predict the outcome of postoperative hypocalcemia.

Conclusions

Clinically significant hypocalcemia following thyroid surgery is secondary to impairment of parathyroid function in most cases. When in situ preservation of parathyroid glands and their blood supply is enforced during thyroidectomy, the incidence of postoperative hypocalcemia and permanent hypoparathyroidism can

be consistently restricted, to less than 10% and 1%, respectively. When facing postoperative hypocalcemia, we found that patients in whom fewer than three parathyroid glands were preserved during surgery, the early serum PTH level was ≤ 12 pg/ml, the delayed serum calcium level was ≤ 8 mg/dl, or the delayed serum phosphorus level was ≥ 4 mg/dl under oral calcium therapy (or any combination of these factors) carried a high risk for permanent hypoparathyroidism. When one or more of these criteria are present, long-term follow-up should be initiated to check for chronic hypocalcemia and to avoid its severe complications by administering appropriate supplement therapy.

Résumé

L'hypocalcémie postopératoire est un événement fréquent et le plus souvent transitoire après chirurgie thyroïdienne étendue. Elle indique souvent des lésions iatrogènes des glandes parathyroïdes et est parfois définitive. Nous avons prospectivement évalué l'incidence de l'hypocalcémie et de l'hypoparathyroïdie définitive après la thyroïdectomie totale ou subtotale chez 1071 patients consécutifs, opérés entre 1990 et 1991. Nous avons ainsi déterminé en étude croisée quels critères cliniques et biochimiques précoces des patients hypocalcémiques prédicteurs de l'évolution à long terme. On a observé une calcémie postopératoire inférieure à 2 mmol/L chez 58 patients (5.7%). Chez 40 patients, l'hypocalcémie a été considérée comme sévère (confirmée pendant plus de deux jours et/ou symptomatique). Un an après chirurgie, 5 patients (0.5%) avaient une hypocalcémie persistante. Nous avons trouvé que les patients chez lesquels on a conservé moins de trois glandes parathyroïdes in situ, et/ou qui avaient un taux de PTH sérique précoce moins que ou égal à 12 pg/ml, et/ou une calcémie retardée égale ou moins de 8 mg/dl, et/ou une phosphorémie retardée égale ou moins de 4 mg/dl sous thérapie calcique, avaient un risque élevé d'hypoparathyroïdie définitive. Lorsqu'un ou plusieurs de ces critères sont présents, il faut préconiser une surveillance prolongée pour vérifier l'absence d'hypocalcémie persistante et éviter complications propres à l'hypocalcémie par un traitement supplémentaire approprié.

Resumen

La hipocalcemia postoperatoria es un fenómeno común y frecuentemente transitorio, que ocurre luego de cirugía extensa de la glándula tiroides. Puede significar lesión yatrogénica de las glándulas paratiroides con hipoparatiroidismo permanente. Hicimos una evaluación prospectiva de la incidencia de hipocalcemia y de hipoparatiroidismo permanente asociado con tiroidectomía subtotal en 1071 pacientes consecutivos, operados entre 1990 y 1991. Mediante un estudio de corte horizontal procedimos a determinar cuáles son las características precoces, clínicas y bioquímicas de los pacientes que desarrollan hipocalcemia postoperatoria, en correlación con el resultado final a largo plazo. Se observó calcemia postoperatorio inferior a 2 mmol/L en 58 pacientes (5.7%), y en 40 la hipocalcemia fue considerada grave (confirmada por más de 2 días y/o sintomática). Al año de la cirugía, 5 pacientes (0.5%) sufrían hipocalcemia persistente. Encontramos que los pacientes en quienes se preservaron in situ menos de 3 glándulas paratiroides en el curso de la cirugía, y/o la determinación temprana de PTH en el suero mostró un valor de 12 pg/ml o menos, y/o los niveles tardíos de calcio sérico fueron de 8 mg/dl o menos, y/o los niveles tardíos de fósforo sérico fueron de 4 mg/dl o menos bajo terapia oral con calcio, conllevan un alto riesgo de hipoparatiroidismo permanente. En presencia de uno o más de estos criterios, es necesario el seguimiento a largo plazo a fin de controlar la hipocalcemia crónica y evitar sus graves complicaciones, mediante una adecuada terapia de suplencia.

References

1. Jacobs, J.K., Aland, J.W., Ballinger, J.F.: Total thyroidectomy: a review of 213 patients. Ann. Surg. *197*:543, 1983
2. Pederson, W.C., Johnson, C.L., Gaskill, H.V., Aust, J.B., Cruz, A.B.: Operative management of thyroid disease: technical considerations in a residency training program. Am. J. Surg. *148*:350, 1984
3. Schwartz, A.E., Friedman, E.W.: Preservation of the parathyroid glands in total thyroidectomy. Surg. Gynecol. Obstet. *165*:327, 1987
4. Peix, J.L., Zabot, J.M.: Complications and consequences of thyroid surgery (in French). Presse Med. *17*:1749, 1988
5. Deard, F., Santini, J., Pepino, J.M.: Subtotal thyroidectomy for multinodular goiter: experiences of 223 cases. Ann. Chir. *42*:735, 1988
6. Kraimps, J.L., Barbier, J., Carretier, M., Babin, P., Jardel, P.: Analysis of a series of 102 carcinomas of the thyroid gland (in French). Sem. Hop. Paris *64*:1423, 1988
7. Tovi, F., Noyek, A.M., Chapnik, J.S., Freeman, J.L.: Safety of total thyroidectomy: review of 100 consecutive cases. Laryngoscope *99*: 1233, 1989
8. Prades, J.M., Bertholon, P., Estour, B., Martin, C.: Risks of thyroid surgery (in French). J. Fr. Otol. Rhinol. Laryngol. (Paris) *39*:479, 1990
9. Proye, C., Carnaille, B., Maynou, C., Bizard, J.P., Gilliot, P., Lariviere, J., Martinot, J.C., Monnin, C., Vallier, F.: Parathyroid risk following thyroid surgery (in French). Chirurgie *116*:493, 1990
10. Megherbi, M.T., Graba, A., Oulmane, D., Saidini, M., Benabadji, R.: Complications et séquelles de la chirurgie thyroïdienne bénigne [Complications of benign thyroid surgery] (in French). J. Chir. (Paris) *129*:41, 1992
11. Olson, J.A., DeBenedetti, M.K., Baumann, D.S., Wells, S.A.: Parathyroid autotransplantation during thyroidectomy: results of long-term follow-up. Ann. Surg. *223*:472, 1996
12. Al-Suliman, N.N., Ryttov, N.F., Qvist, N., Blichert-Toft, M., Graversen, H.A.: Experience in a specialist thyroid surgery unit: a demographic study, surgical complications, and outcome. Eur. J. Surg. *163*:13, 1997
13. Demeester-Mirkine, N., Hooghe, L., Van Geertruyden, J., de Maertelaer, V.: Hypocalcemia after thyroidectomy. Arch. Surg. *127*:854, 1992
14. Wilkin, T.J., Paterson, C.R., Isles, T.E., Crooks, J., Swanson Beck, J.: Post-thyroidectomy hypocalcaemia: a feature of the operation or the thyroid disorder. Lancet *1*:621, 1977
15. Michie, W., Duncan, T., Hamer-Hogdges, D.W., Bewsher, P.D., Stowers, J.M., Pegg, C.A.S., Hedley, A.J.: Mechanism of hypocalcaemia after thyroidectomy for thyrotoxicosis. Lancet *1*:508, 1971
16. Bellamy, R.J., Kendall-Taylor, P.: Unrecognized hypocalcaemia diagnosed 36 years after thyroidectomy. J. R. Soc. Med. *88*:690, 1995
17. Reber, P.M., Heath, H.: Hypocalcemic emergencies. Med. Clin. North Am. *79*:93, 1995
18. Proye, C., Maes, B., Bondil, P., Vanseymortier, L., Lagache, G.: Reality and prevention: 502 bilateral thyroidectomy (in French). Chirurgie *119*:491, 1982
19. McHenry, C.R., Speroff, T., Wentworth, D., Murphy, T.: Risk factors for post-thyroidectomy hypocalcemia. Surgery *116*:641, 1994
20. Nobori, M., Saiki, S., Tanaka, N., Harihara, Y., Shindo, S., Fujimoto, Y.: Blood supply of the parathyroid gland from the superior thyroid artery. Surgery *115*:417, 1994
21. Percival, R.C., Hargreaves, A.W., Kanis, J.A.: The mechanism of hypocalcemia following thyroidectomy. Acta Endocrinol. (Copenh.) *109*:220, 1985
22. Michie, W., Stowers, J.M., Frazer, S.C.: Post-thyroidectomy hypocalcemia. Lancet *1*:1051, 1977
23. See, A.C.H., Soo, K.C.: Hypocalcaemia following thyroidectomy for thyrotoxicosis. Br. J. Surg. *84*:95, 1997

24. Laitinen, O.: Hypocalcemia after thyroidectomy. Lancet *2*:859, 1976
25. Öhman, U., Granberg, P.O., Lindell, B.: Function of the parathyroid glands after total thyroidectomy. Surg. Gynecol. Obstet. *146*:773, 1978
26. Hans, S.S., Tai Lee, P.: Post-thyroidectomy hypoparathyroidism. Am. Surg. *42*:930, 1976
27. Prigouris, S., Lorentziadis, M., Stylogiannis, S., Nafas, R., Masouras, A., Poulantzas, I.: Experimental autotransplantation of the parathyroid gland. Br. J. Surg. *83*:410, 1996

Invited Commentary

Tom Reeve, M.D.

Endocrine Surgical Unit, Sydney University, Royal North Shore Hospital and Australian Cancer Network, Sydney, Australia

Surgeons sometimes operate to ameliorate a pathologic condition, aiming to correct it, but while doing so iatrogenically cause another disease. In such situations, on the face of it such surgical practice must be considered far from ideal.

As outlined by Pattou et al., hypocalcemia following thyroidectomy is usually, but not always, iatrogenic in origin. Although improving the technical aspects of thyroidectomy through training and meticulous practice has led to a significant decrease in permanent hypoparathyroidism after thyroidectomy [1, 2], the problem of permanent hypoparathyroidism remains a serious matter, requiring attention from all surgeons who operate on the thyroid gland.

This longitudinal and cross-sectional study combined with the careful surgical protocols followed by the authors provides results equivalent to those reported by endocrine surgical units pursuing excellence around the world [1]. However, all units still have some problems with transient hypocalcemia and permanent hypoparathyroidism. These complications have assumed even greater significance now that time and cost factors have such a significant place in surgical practice [1, 3]. An important situation where cost is incurred is in training surgeons, but this is a cost that seems well justified [4].

The authors appear to have had less success with autotransplantation than others [5]. To overcome this problem, they have paid close attention to the vascular supply of the parathyroid glands and preserved them in situ. This practice sometimes leads to significant dissection time. Moreover, even with preservation of a small amount of thyroid at the upper pole to protect the anastomatic or direct blood supply from the superior thyroid artery [6, 7], the parathyroid glands may still have deficient blood supply. A recent trial in our unit (Zedenius, personal communication) of routine autotransplantation of any visually suspect parathyroid gland (after incision of the capsule to determine vascular flow), or at least one normal parathyroid gland, has resulted in no permanent hypoparathyroidism after 100 successive total thyroidectomies in contrast to a rate of 0.3% before this practice became policy in our unit.

No patient should leave the hospital at risk of acute hypocalcemia without some protective steps with supplementary calcium or vitamin D derivatives. Until early predictive criteria are established and clinical criteria become available, the criteria listed in by Pattou et al. in their Table 4 should alert surgeons to patients who may be experiencing serious hypocalcemia.

References

1. Al-Suliman, N.N., Ryltov, N.F., Qvist, N., Blichert-Toft, M., Graversch, H.P.: Experience in a specialist thyroid surgery unit: a demographic study, surgical complications and outcome. Eur. J. Surg. *163*:13, 1997
2. Reeve, T.S., Curtin, A., Fingleton, L., Kennedy, C., Mackie, W., Porter, T., Simons, D., Delbridge, L.: Can total thyroidectomy be performed as safely by general surgeons in provincial areas as by surgeons in specialised endocrine surgical units? Arch. Surg. *129*:834, 1994
3. McHenry, C.R., Speroff, T., Wentworth, D., Murphy, T.: Risk factors for post thyroidectomy hypocalcaemia. Surgery *116*:641, 1994
4. Martin, L., Delbridge, L., Martin, J., Grimmer, P., Poole, A.G., Reeve, T.S.: Trainee surgery: is there a cost? Aust. N.Z. J. Surg. *59*:257, 1989
5. Olson, J.A., DeBennelti, M.I., Baumann, D.S., Wells, S.A.: Parathyroid autotransplantation during thyroidectomy: results of long term follow up. Ann. Surg. *223*:472, 1996
6. Nobori, M., Saiki, S., Tanaka Harihare, Y., Shindo, S., Fujimoto, Y.: Blood supply of the parathyroid gland from the superior thyroid artery. Surgery *115*:417, 1994
7. Hunt, P.S., Poole, M., Reeve, T.S.: Reappraisal of the surgical anatomy of the thyroid and parathyroid glands. Br. J. Surg. *63*:55, 1968