

Parathyroid risk in total thyroidectomy for bilateral, benign, multinodular goitre: report of 351 surgical cases

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Abstract

Aims: To evaluate the risk of hypocalcaemia (transient or permanent) after total thyroidectomy for bilateral, benign, multinodular goitre, the frequency and impact of unintentional parathyroidectomy, and the value of parathyroid gland autotransplantation during thyroid surgery.

Materials and methods: This was a retrospective study of 351 surgical patients who had undergone total thyroidectomy for bilateral, benign, multinodular goitre over a seven-year period. The primary endpoint was serum calcium concentration immediately post-operatively and during follow up. Normal serum calcium concentration was defined as 2 mmol/l. Parathyroid data were collected during surgery and histological examination.

Results: In 62 per cent of cases, no hypocalcaemia had been observed after surgery. In 35 per cent of cases, transient hypocalcaemia had been observed after surgery. In 3 per cent of cases, chronic hypocalcaemia had been present six months after surgery. Permanent hypoparathyroidism had been diagnosed two years after surgery in 1.4 per cent of cases. Unintentional parathyroidectomy had been detected in 5.2 per cent of cases. Parathyroid gland autotransplantation had been performed in 7 per cent of cases during surgery.

Conclusion: Permanent hypoparathyroidism is rare, although transient hypoparathyroidism occurs relatively frequently. Unintentional parathyroidectomy and parathyroid gland autotransplantation do not affect serum calcium levels.

Key words: Thyroid Surgery; Hypocalcaemia; Parathyroid Gland; Complications

Introduction

Several anatomical considerations must be taken into account during thyroid surgery: the arteries and veins of the thyroid gland; the position of the parathyroid glands; and the position of the laryngeal nerves. The most significant complication is recurrent laryngeal nerve palsy, which can cause severe dysphonia and dysphagia, with serious social repercussions. However, permanent hypoparathyroidism is another serious complication which can sometimes be difficult to manage.

This study, based on 351 patients undergoing total thyroidectomy for bilateral, benign, multinodular goitre, was designed to evaluate serum calcium levels after total thyroidectomy, to analyse the frequency of unintentional parathyroidectomy, and to analyse the efficacy of parathyroid gland autotransplantation.

Materials and methods

Population

This was a retrospective study of 351 patients (281 women and 70 men) who had undergone total

thyroidectomy for bilateral, benign, multinodular goitre over a seven-year period (from January 1995 to December 2002).

No patients with thyroid cancer or Grave's disease, or any who had undergone thyroid re-operations, were included in this study.

Post-operative serum calcium

Total serum calcium concentration had been evaluated during the first three post-operative days, on the 15th post-operative day and thereafter as justified by the results of previous assays.

Hypocalcaemia was defined as a serum calcium concentration of less than 2 mmol/l, while a serum calcium concentration of greater than 2 mmol/l was considered normal.

Hypocalcaemia was classified into four types: labile hypocalcaemia (i.e. hypocalcaemia lasting less than a fortnight); transient hypocalcaemia (i.e. hypocalcaemia returning to normal within six months of surgery); chronic hypocalcaemia (hypocalcaemia persisting six months after surgery); and permanent hypoparathyroidism (hypocalcaemia persisting two years after surgery).

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Oral calcium supplements

Patients with symptomatic hypocalcaemia and a serum calcium concentration of above 1.85 mmol/l had been treated with an oral calcium supplement (3 g per day). Patients with hypocalcaemia and a serum calcium concentration of less than 1.85 mmol/l had almost always been symptomatic and had been treated with oral vitamin D (alfacalcidol 0.25 µg thrice per day) and calcium (3 g per day) supplements.

Surgical procedure

All patients had undergone total thyroidectomy via a small cervical incision.

Sternotomy had never been performed, nor had lymph node dissection along the recurrent laryngeal nerve.

Thyroid lobectomies had been performed in a caudocranial direction by capsular dissection, after first identifying the recurrent laryngeal nerve. Parathyroid glands had been identified and preserved, together with their internal blood supply, whenever possible.

When the parathyroid gland had been devascularized during surgery, parathyroid gland autotransplantation had always been performed onto the sternocleidomastoid muscle in two or three sites, after separation of the resected parathyroid glands.

Results

Identification of parathyroid glands during surgery

The superior parathyroid gland had been more frequently identified during surgery (69 per cent of cases) than the inferior gland (31 per cent of cases), with no significant difference between the two sides.

A variable number of parathyroid glands had been identified during surgery (Table I). One or two parathyroid glands had been identified in 175 patients (50 per cent of cases) and three or four parathyroid glands in 144 patients (41 per cent of cases). No parathyroid gland had been identified in 32 patients (9 per cent of cases).

Post-operative serum calcium

An assessment of the kinetics of serum calcium concentration decline demonstrated transient hypocalcaemia that lasted less than a fortnight. Hypocalcaemia which returned to normal before the sixth month after surgery was considered transitory hypocalcaemia. Beyond that date, chronic and persistent hypocalcaemia was said to be present, often

indicative of probable permanent hypoparathyroidism. Nevertheless, patients suspected of permanent hypoparathyroidism had been followed for up to two years after surgery, with regular serum calcium testing. Hypocalcaemia persisting two years after surgery was considered definitive (i.e. definite hypoparathyroidism).

Clinical symptoms of hypocalcaemia had appeared when the blood calcium level was less than 1.85 mmol/l and had essentially been characterized by paraesthesia (numbness or tingling around the mouth or in the feet and hands) and (sometimes) by muscle spasms in the face, feet and hands. In cases of hypocalcaemia of less than 1.65 mmol/l, a tachycardia or tetany may be observed.

In 216 cases (62 per cent), the serum calcium concentration had remained normal after surgery (Table II).

Labile or transient hypocalcaemia had been observed in 123 cases (35 per cent). Twenty-four per cent of patients had experienced paraesthesia; 32 per cent of these were treated with oral calcium supplements and 17.5 per cent with oral calcium and vitamin D supplements. The post-operative serum calcium concentration had returned to normal over 15 to 30 days in 65 per cent of cases and over one to six months in 35 per cent of cases.

Twelve cases (3 per cent) had developed chronic hypocalcaemia, which corresponded to permanent hypoparathyroidism in 1.7 per cent of cases.

Detailed analysis of the cases of chronic hypocalcaemia revealed the following findings. One patient had died within seven months from non-thyroid cancer. In five cases, parathyroid function had recovered 18 months after the operation, with maintenance of a normal serum calcium level after discontinuation of treatment. In six cases, permanent hypoparathyroidism had been diagnosed two years after surgery. In these six cases, serum calcium levels had remained unstable at less than 2 mmol/l, despite oral calcium and vitamin D supplements, and had rapidly declined when treatment was stopped. Five of these six cases had presented clinical symptoms of hypoparathyroidism. One patient had remained asymptomatic but with unstable serum calcium levels. One patient had experienced intermittent paraesthesia, with a serum calcium level of 1.94 mmol/l and a serum parathormone level of 13 mg/l (normal level, 13–26 mg/l). Two of the treated patients had tolerated oral calcium supplements poorly.

TABLE I

NUMBER OF PARATHYROID GLANDS IDENTIFIED DURING SURGERY	
Parathyroid glands (<i>n</i>)	%*
4	8
3	33
2	31
1	19
0	9

*Of cases.

TABLE II

POST-OPERATIVE SERUM CALCIUM LEVEL	
Post-op serum Ca (mmol/l)	%*
>2	61.5
1.9–2	13.7
1.8–1.9	13.5
1.7–1.8	5.7
1.6–1.7	2.9
1.5–1.6	2.7

*Of cases. Post-op = post-operative

Correlation between parathyroid identification during surgery and post-operative hypocalcaemia

No correlation was demonstrated between post-operative hypocalcaemia and the number of parathyroid glands which had been identified during surgery.

Among the 216 patients with normal serum calcium after surgery, no parathyroid gland had been identified in 15 cases (7 per cent), one or two parathyroid glands in 113 cases (52 per cent) and three or four parathyroid glands in 88 cases (41 per cent).

Among the 123 patients with labile or transient post-operative hypocalcaemia, no parathyroid gland had been identified in 15 cases (12 per cent), one or two parathyroids in 62 cases (50 per cent), and three or four parathyroids in 46 cases (48 per cent).

Among the 12 patients with chronic hypocalcaemia or permanent hypoparathyroidism following surgery, no parathyroid gland had been identified in two cases (17 per cent) and three or four parathyroid glands in 10 cases (83 per cent).

Unintentional parathyroidectomy

Unintentional parathyroidectomy had occurred in 22 cases (5.2 per cent of cases).

In these 22 cases, detailed identification of parathyroid glands during surgery had occurred as follows: no parathyroid gland in three cases; two parathyroids in nine cases; three parathyroids in six cases and four parathyroids in four cases.

Histological examination of unintentional parathyroidectomies had revealed that 17 parathyroids had been extracapsular and five had been intracapsular within the thyroid gland.

Unintentional parathyroidectomy had had no impact on post-operative serum calcium concentration in 15 of these 22 cases.

Transient hypocalcaemia had been observed in seven cases: five with a serum calcium level between 1.85 and 2 mmol/l, and two with a serum calcium level of 1.73–1.8 mmol/l. No cases of chronic hypocalcaemia or permanent hypoparathyroidism had been observed.

Parathyroid gland autotransplantation

Parathyroid gland autotransplantation had been performed in 5.7 per cent of cases. The parathyroid glands had always been transplanted into the sternocleidomastoid muscle, in two or three sites, after division of the resected parathyroids. This had usually involved a devascularized, dissected out

parathyroid gland. In all cases of autotransplantation, the post-operative serum calcium level had either remained normal or transiently decreased for the first fortnight, preventing functional evaluation of the transplanted parathyroid but suggesting that a sufficient amount of parathyroid tissue had been left in place.

Discussion

The incidence of post-operative hypoparathyroidism has increased in our experience, as a result of changes in our surgical management of thyroid gland disease.

Before 1994, total thyroidectomies had represented 40 per cent of all thyroid resections, while subtotal thyroidectomies had represented 20 per cent and lobectomy plus isthmectomy 40 per cent. Note that the incidence of post-operative hypoparathyroidism had been the same after subtotal thyroidectomy and total thyroidectomy. The subtotal thyroidectomy technique was no more effective at preserving the blood supply of the superior parathyroid glands than was the total thyroidectomy procedure. After 1994, subtotal thyroidectomies were abandoned in favour of total thyroidectomies, which then represented nearly 60 per cent of all surgical procedures. Over recent years, the frequency of total thyroidectomy has increased and now represents nearly 80 per cent of all thyroidectomy procedures. The extent of thyroid dissection when performing total thyroidectomy increases the risk of damage to the parathyroid glands and to their blood supply. Surgical experience and a meticulous surgical technique are the two mainstays of improvement of the quality of thyroid surgery. In our series, only two of the 15 cases of chronic hypoparathyroidism occurred after 2000.

Unintentional parathyroidectomy

Few studies have assessed the incidence of unintentional parathyroidectomy (Table III).

The incidence of unintentional parathyroidectomy ranges from 1 to 15 per cent, and all authors confirm that unintentional parathyroidectomy has no impact on post-operative serum calcium (Table III). Lin *et al.*³ found that unintentional parathyroidectomy mostly occurred in the context of re-operations and recurrent lymphadenectomy but did not have any impact on post-operative serum calcium. Debry *et al.*,⁴ in a series of 588 thyroidectomies (42 per cent of which were total thyroidectomies), found an

TABLE III
FREQUENCY OF UNINTENTIONAL PARATHYROIDECTOMY

Author	Patients (n)	Unintentional parathyroidectomy (%)	Intrathyroid (%)	Extrathyroid (%)	Effect on serum Ca
Sasson <i>et al.</i> ¹	141	15	50	31	None
Muller <i>et al.</i> ²	414	11	58	42	None
Lin <i>et al.</i> ³	220	9	–	–	None
Debry <i>et al.</i> ⁴	588	1	–	–	None
Bergamashi <i>et al.</i> ⁵	1192	9	–	–	None

unintentional parathyroidectomy incidence of only 1 per cent. Bergamashi *et al.*,⁵ in a series of 1192 thyroidectomies, found an unintentional parathyroidectomy incidence of 9 per cent and performed parathyroid gland autotransplantation in 19 per cent of cases. Our 351 patients constitute a homogeneous series, since total thyroidectomy was performed for benign disease in every case.

Unintentional parathyroidectomy is easier to understand in the case of intrathyroid parathyroids, for which the unintentional parathyroidectomy rate ranges from 50 per cent (Muller *et al.*)² to 20 per cent in our group. However, unintentional parathyroidectomy can be considered to be a surgical error when the parathyroid glands are extracapsular. For example, a small parathyroid gland may extend over the thyroid parenchyma with a thick and inflammatory capsule. Sometimes, the parathyroid gland is situated between two nodular expansions of the goitre. Recurrent neck dissections predispose to unintentional parathyroidectomy when the parathyroids are not identified prior to resection, especially when neck dissection is bilateral and in the presence of recurrent lymph nodes. The low incidence of unintentional parathyroidectomy in the literature may also reflect the absence of histological examination of the entire operative specimen. The impact of unintentional parathyroidectomy on serum calcium levels is minor when only one parathyroid gland is concerned, with the other parathyroid glands being preserved. However, unintentional parathyroidectomy of two glands can be responsible for permanent hypoparathyroidism when the blood supply to the other parathyroids has been damaged.

Post-operative serum calcium

A large number of papers on hypoparathyroidism after thyroidectomy have been published.^{4–11} However, accurate meta-analysis is difficult because of the lack of standard criteria for hypocalcaemia levels or post-operative timeframes for the diagnosis of permanent hypoparathyroidism. For example, a six-month post-operative period is often used to define permanent hypoparathyroidism. However, five cases in our study recovered 18 months after the operation. A high incidence of transient and permanent hypocalcaemia is reported in the literature. Transient hypocalcaemia is observed in 2 to 23 per cent of cases and permanent hypocalcaemia in 0 to 5 per cent of cases (Table IV).

Identification of the parathyroid glands during surgery varies according to the surgical technique, the disease treated and the surgical difficulty. Some authors, such as Coudray,⁸ systematically locate the parathyroid glands, while others do not. We believe that juxtacapsular dissection of the thyroid gland with ligation of small vessels is the best way to preserve the parathyroid glands and their blood supply. We also believe that it is preferable to identify the parathyroids during the course of dissection, rather than to deliberately try to locate them when systematically performing the dissection towards the recurrent laryngeal nerve. Particular caution is required close to the superior parathyroid gland, which is often situated close to the recurrent laryngeal nerve (and particularly close to the point at which it enters the larynx) and the branches of the inferior thyroid artery. The inferior parathyroid gland often lies in the fatty tissue at the inferior part of the thyroid lobe or within the thyrothymic ligament and should therefore not be damaged when the thyroid gland dissection is 'capsular'.

At the end of the operation, the surgical zone should be carefully inspected. If a parathyroid gland has been removed with the thyroid parenchyma, autotransplantation into the sternocleidomastoid muscle is imperative after a floating test in serum or following frozen section histological examination of a small fragment.¹² At the end of the operation, the remaining parathyroid glands should be inspected to assess their viability. If persistent ischaemia is observed, autotransplantation should be performed. Transient hypocalcaemia often appears because of a vascular spasm of the parathyroid gland, and permanent hypocalcaemia can occur as a result of devascularization. Rare cases of hypocalcaemia may be due to a congenital defect affecting the number of parathyroid glands. However, a normal serum calcium level despite the high rate of unintentional parathyroidectomy could possibly be explained by supernumerary parathyroid glands located away from the thyroid region. These speculative arguments are difficult to prove, although anatomical studies of a few cases have revealed more or less than four parathyroid glands.

Surgical experience may reduce the frequency of hypoparathyroidism. For example, Seiler¹³ performed 3193 thyroidectomies from 1972 to 1996 and defined two phases: a first phase with a 3.6 per cent permanent hypocalcaemia rate, followed by a

TABLE IV
POST-OPERATIVE HYPOCALCAEMIA AFTER THYROID SURGERY

Author	Patients (n)	Transient hypocalcaemia (%)	Permanent hypocalcaemia (%)
Muller <i>et al.</i> ⁶	913	2	0.5
La Gamma <i>et al.</i> ⁷	178	19	3.6
Coudray <i>et al.</i> ⁸	538	23	2
Giovannini <i>et al.</i> ⁹	337	13.6	0
Bergamashi <i>et al.</i> ⁵	1192	20	4
Pons Rocher <i>et al.</i> ¹⁰	683	22.7	5.3
Rosato <i>et al.</i> ¹¹	300	8.3	2

second phase with a 1 per cent permanent hypocalcaemia rate. Some thyroid diseases and surgical techniques may impair parathyroid function. Grave's disease, substernal goitre, cancer and re-operations increase the incidence of post-operative hypocalcaemia.⁴ Makaieff *et al.*¹⁴ reported a 4.6 per cent incidence of permanent hypoparathyroidism after 117 re-operations and a 2.1 per cent incidence after surgery on 220 substernal goitres. In a series of 180 cases of thyroid cancer, Schwartz and Friedman¹⁵ reported a 2.3 per cent permanent hypoparathyroidism rate. Sim and Soo¹⁶ reported a rate of 3.4 per cent in 149 cases. Hundahl *et al.*¹⁷ reported a rate of 10 per cent in 5583 cancer cases operated upon in 1996.

- **Several anatomical considerations must be taken into account during thyroid surgery: the arteries and veins of the thyroid gland; the position of the parathyroid glands; and the position of the laryngeal nerves**
- **Permanent hypoparathyroidism is a serious complication that can sometimes be difficult to manage**
- **This was a retrospective study of 351 surgical patients undergoing total thyroidectomy for bilateral, benign, multinodular goitre over a seven-year period**
- **Permanent hypoparathyroidism is rare, although transient hypoparathyroidism is relatively frequent. Unintentional parathyroidectomy and parathyroid gland autotransplantation do not affect serum calcium levels**

Coudray *et al.*⁸ performed 52 cases of autotransplantation; this involved the forearm in 6.7 per cent of cases, the neck in 24 per cent of cases and both in 9 per cent of cases. No difference in recovery of serum calcium concentration was observed between the group with autotransplanted parathyroid glands and the group without autotransplanted parathyroid glands.

Conclusion

The incidence of permanent hypoparathyroidism after thyroid surgery ranges from 0 to 5 per cent of cases. In our series of 351 benign goitres, the incidence was 1.4 per cent of cases.

The incidence of chronic hypoparathyroidism can be reduced by a meticulous surgical technique and surgical experience. However, despite a careful surgical procedure, transient hypocalcaemia is frequently observed because of the fragile blood supply of the parathyroid glands. The risk of permanent hypoparathyroidism is increased in cases of thyroid cancer, Grave's disease and re-operation.

Before surgery, patients must be informed about the possibility of transient or permanent hypocalcaemia as well as the chance of recurrent laryngeal nerve palsy.

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