



Parathyroid Autotransplantation during Total Thyroidectomy—Does the Number of Glands Transplanted Affect Outcome?

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Abstract. Parathyroid autotransplantation is a technique for ensuring the continued function of parathyroid tissue at the time of total thyroidectomy (TT). The aim of this study was to ascertain whether the number of parathyroids transplanted affects the incidence of temporary and permanent hypoparathyroidism. A retrospective cohort study included all patients undergoing a TT in a single unit between July 1998 and June 2003. The number of parathyroids transplanted, the final pathology, and the incidence of temporary and permanent hypoparathyroidism were documented. Fisher's exact test was used for statistical analysis. A total of 1196 patients underwent a TT during the 5 years studied. Of these, 306 (25.6%) had no parathyroids transplanted, 650 (54.3%), 206 (17.2%), 34 (2.8%) had 1, 2, or 3 glands autotransplanted, respectively. The incidence of temporary hypoparathyroidism was 9.8% for no gland transplants, 11.9%, 15.1%, and 31.4% for 1, 2, and 3 gland transplants, respectively ($p < 0.05$). The incidence of permanent hypoparathyroidism was 0.98%, 0.77%, 0.97%, and 0%, respectively ($p = NS$). The incidence of temporary hypoparathyroidism was higher when surgery was performed for Graves' disease. Temporary hypocalcemia is closely related to the number of autotransplanted parathyroids during TT. The long-term outcome is not affected by the number of parathyroids autotransplanted. A "ready selective" approach to parathyroid autotransplantation is an effective strategy for minimizing the rate of permanent hypoparathyroidism.

edema despite meticulous dissection [3]. Furthermore, occasionally parathyroid glands may be inadvertently removed with the thyroid specimen during surgery because they were not identified intra operatively. The process of parathyroid autotransplantation during a partial thyroidectomy was first described by Lahey [4]. However, only after the demonstration of the viability of transplanted parathyroid tissue in humans [5] did autotransplantation become part of the endocrine surgical armamentarium. Most surgeons would accept that when preservation of parathyroid tissue in situ is not an option the best alternative is parathyroid autotransplantation (PAT) [6]. However, the adoption of PAT by endocrine surgeons has varied considerably from a selective approach with transplantation of nonviable glands [7] to routine autotransplantation of one gland [8] to autotransplantation of all identifiable parathyroids or at least two of the identified glands [9].

The aim of this study was to identify whether the number of parathyroids autotransplanted has an effect on the incidence of permanent hypoparathyroidism or the incidence of temporary hypocalcemia.

Permanent hypoparathyroidism following thyroid surgery is a potentially debilitating condition. Fears of permanent hypoparathyroidism have in the past led many surgeons to adopt subtotal thyroidectomy as their standard procedure for benign thyroid disease. However, it is increasingly recognized that total rather than subtotal thyroidectomy is the optimal procedure for benign multinodular goiters [1], as well as for all but the lowest risk thyroid cancers [2]. This has renewed the interest in the need for parathyroid preservation during thyroidectomy.

The preservation of as much functional parathyroid tissue in situ as possible is the key to minimizing permanent hypoparathyroidism. However, some glands may be anatomically intact but not physiologically viable, either because of thrombosis of the delicate parathyroid artery or because of parathyroid capsule

Methods

A retrospective cohort study comprising all patients that had a total thyroidectomy (TT) between July 1998 and June 2003 was performed. Data were obtained from the Endocrine Surgery database, which is prospectively compiled and regularly audited for accuracy. For each TT, the number of parathyroids transplanted, the histopathology, and the incidence of temporary hypocalcemia and permanent hypoparathyroidism were documented.

For the purposes of this study temporary hypocalcemia was defined as any patient with corrected serum calcium of less than 2 mmol/l, with or without symptoms, that returned to the normal range at 3 months follow-up without requiring calcium supplementation. Permanent hypoparathyroidism was defined as any patient with a serum calcium level below the normal range or requiring calcium and/or vitamin D supplementation to remain eucalcaemic at 6 months from surgery.

Table 1. Histopathology and numbers of patients undergoing total thyroidectomy in the 5 years 1998–2003.

Pathology/indications	Number
MNG	636
Carcinoma	238
Graves' disease	144
Hashimoto's thyroiditis	48
Follicular adenoma	41
Hurtle cell adenoma	7
Colloid nodule	6
Sub acute thyroiditis	2
Simple cyst	2
Unknown/ combined pathologies	72

Table 2. Relationship between the incidence of temporary hypocalcemia and number of transplanted parathyroids following a total thyroidectomy.

Number of glands transplanted	Ratio of temporary hypocalcemia / total patients	Incidence temporary hypocalcemia	<i>p</i> Value
0	30/306	9.8%	
1	77/650	11.9%	0.38
2	31/206	15.1%	0.05
3	11/34	35.1%	0.001

Data were analyzed using the Stata Statistical Software package (version 7, Stata Corp, College Station, TX). Comparison of the rate of hypocalcemia and hypoparathyroidism was performed using Fisher's exact test. The Alpha for significance was set at $p < 0.05$

Results

A total of 1196 patients underwent TT in the University of Sydney Endocrine Surgery Unit in the 5 years between July 1998 and June 2003 with the indications for surgery and/or histopathology as documented in Table 1. Of these 306 (25.6%) had no parathyroid glands transplanted, 650 (54.3%) had 1 gland autotransplanted, 206 (17.2%) had 2 glands autotransplanted, and 34 (2.9%) had 3 glands autotransplanted.

Overall, 149 (12.5%) patients experienced temporary hypocalcemia after TT, with a statistically significant increase in incidence as the number of glands transplanted increased (Table 2).

The incidence of temporary hypocalcemia was higher in patients with Graves' disease regardless of the number of parathyroid glands transplanted, although this difference became less marked as the number of parathyroid transplants increased. The incidence of permanent hypoparathyroidism in thyrotoxic patients was not significantly different from the overall incidence (Table 3).

Overall, there were 10 cases of permanent hypoparathyroidism after TT over 5 years and 1197 operations (0.84%). There were 3 cases in patients that had no PAT (0.98%), 5 cases in patients that had had one parathyroid transplanted (0.77%), 2 cases in patients that had two glands transplanted (0.97%), and no cases in patients that had three glands transplanted. These differences were not statistically significant.

Discussion:

Thyroid disease is prevalent [10], and over 8,200 primary thyroid operations are typically performed each year in the UK [11] and

just over 4100 were performed over twelve months in Australia from 2002 to 2003. However, thyroidectomy continues to produce significant morbidity. In 1989 4% of all surgical claims settled by the Medical Defence Union in the UK [12], and 1% of all litigation relating to adverse effects after medical or surgical treatment in Germany between 1975 and 1998 were related to thyroid surgery [13]. After recurrent laryngeal nerve palsy, permanent hypoparathyroidism accounts for the largest category of thyroidectomy-related claims [12]. Because adverse events tend to be under reported in the literature, the true incidence of permanent hypoparathyroidism is difficult to ascertain, but incidences as low as 0% and as high as 43% have been reported [14]. Permanent hypoparathyroidism is a complication that commits the patient to lifelong calcium and vitamin D supplementation. It has been long known that chronic hypoparathyroidism is associated with an increased risk of cataract formation [15] and calcification of the basal ganglia [16], but reversible peripheral neuropathy [17] and cardiac pathology [18] may also occur. To reduce the risk of permanent hypoparathyroidism, many surgeons adopted a compromise operation in the form of subtotal thyroidectomy as their standard procedure for benign multinodular goiter and Graves' disease. It is now accepted, however, that total rather than subtotal thyroidectomy is the optimal procedure for both benign multinodular goiter [1] and all the but the most low risk thyroid cancers [2]. This has led to a resurgence in interest in the need for parathyroid preservation.

The preservation of as much functional parathyroid tissue in situ as possible during TT is the key to minimizing permanent hypoparathyroidism. This may be accomplished by a combination of preservation of the delicate parathyroid vasculature and ligation of the branches of the inferior thyroid artery as close as possible to the thyroid capsule. Despite the adoption of this approach, some glands maybe anatomically intact but not physiologically viable [9]. Indeed, time-consuming meticulous dissection to preserve functioning parathyroid glands in all cases is destined to fail in some either from thrombosis of the parathyroid artery or parathyroid capsule edema [3]. It can be difficult to ascertain the viability of an apparently anatomically intact parathyroid, and various methods of assessment have been adopted including the careful incision of the parathyroid capsule to assess for bleeding (the knife test) [19], Doppler measurements of the parathyroid vessels [20], and intraoperative parathyroid hormone (PTH) assays [21]. Furthermore, the unintentional removal of parathyroid tissue during thyroidectomy is well documented [22].

There is no question that the use of PAT can be associated with a low incidence of permanent hypoparathyroidism [14], but the cause-effect relationship is difficult to prove, because any approach adopted is probably a reflection of the skill and judgment of the surgeon adopting the technique rather than of the technique *per se*. Within our unit there has been a progressive evolution in the approach to PAT. Early on, PAT was rarely performed, but by the late 1980s the protocol called for a selective approach; i.e., only nonviable glands were transplanted. In the mid 1990s a policy of routine autotransplantation of one gland was introduced in an effort to reduce our incidence of hypoparathyroidism further [23]. Our cumulative experience has demonstrated that the removal of a well vascularized and otherwise normal parathyroid gland is unnecessary because it does not have a positive effect on the incidence of permanent hypoparathyroidism. For this reason a policy of "ready selective" PAT has

Table 3. The incidence of temporary and permanent hypoparathyroidism following total thyroidectomy in toxic and nontoxic glands.

Number of PT transplants	Temporary hypocalcaemia		Permanent hypoparathyroidism	
	Graves ^a	Non Graves ^a	Graves ^a	Non Graves ^a
0	15.2% (5/33)	9.2% (25/273)	0% (0/33)	1.1% (3/273)
1	19.3% (16/83)	10.8% (61/567)	0% (0/83)	0.88% (5/567)
2	36.8% (7/19)	12.8% (24/187)	0% (0/19)	1.07% (2/187)
3	55.6% (5/9)	42.3% (11/25)	0% (0/9)	0% (0/25)

been followed. This consists in the adoption of a low threshold for PAT when it is deemed that time-consuming dissection of the pedicle offers little chance of successfully preserving a functional parathyroid gland.

The efficacy of PAT may be inferred from our data that demonstrate the maintenance of normal serum calcium after the initial period of hypocalcemia. Proof that the grafted parathyroid tissue contributes to the restoration of eucalcemia along with the anatomically and physiologically intact parathyroid left *in situ* is more challenging because parathyroids are normally transplanted in the sternocleidomastoid muscle, and differentiating between graft function and the function of intact parathyroid glands is not accurate [24]. There are however, data from a series of 32 MEN 2A and 2B children who underwent prophylactic parathyroidectomy during a total thyroidectomy. These data reveal that 3 months after a period of postoperative hypocalcemia, normal calcium metabolism was restored in nearly all children [25]

Our data also confirm that PAT is associated with a higher incidence of temporary hypoparathyroidism, as has been previously documented [26]. We have also demonstrated that there is a correlation between the numbers of parathyroids transplanted and the incidence of temporary hypocalcemia. Our results with thyrotoxic patients concur with existing data demonstrating a higher incidence of temporary hypocalcemia in hyperthyroid patients, probably related to skeletal avidity for calcium associated with this pathology [27]. Indeed, there appears to be a correlation between temporary postoperative hypocalcemia and free thyroxine levels [28].

Significantly, the rate of permanent hypoparathyroidism is not a product of the number of glands transplanted at the time of surgery. Indeed, there were no cases of permanent hypoparathyroidism even when three glands were transplanted. This suggests that although there is no need to pursue the policy of routine PAT of at least one gland at every operation, it is a valid technique when a gland is judged to have been compromised or is likely to be compromised by the attempt to dissect the gland free. Adopted judiciously a “ready selective” PAT approach contributes to maintaining an overall incidence of permanent hypoparathyroidism below 1%, regardless of the number of glands transplanted.

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