

Routine Parathyroid Autotransplantation during Total Thyroidectomy: Prospective Study of the Outcomes

Dr. Ashok Kshirsagar¹, Dr. Nitin Nangare², Dr. Aditya Phadke³, Dr. Mahesh Reddy⁴, Dr. Shruti Panickar⁵,
Dr. Madhavendra Kabra⁶, Dr. Ujwal Kumar⁷

¹Professor, Dept of Surgery, Krishna Hospital, Karad, Maharashtra, India

²Assistant Professor, Dept of Surgery, Krishna Hospital, Karad, Maharashtra, India

³Resident, Dept of Surgery, Krishna Hospital, Karad, Maharashtra, India

⁴Resident, Dept of Surgery, Krishna Hospital, Karad, Maharashtra, India

⁵Resident, Dept of Surgery, Krishna Hospital, Karad, Maharashtra, India

⁶Resident, Dept of Surgery, Krishna Hospital, Karad, Maharashtra, India

⁷Resident, 7dept of Surgery, Krishna Hospital, Karad, Maharashtra, India

Abstract: ***Objective:** To compare parathyroid gland autotransplantation with parathyroid gland preservation in situ with respect to the preservation of parathyroid gland function in patients undergoing total thyroidectomy. **Methods:** The quasi-experimental study was performed from July 2004 to June 2015 at the Krishna Hospital, Karad. A total of 388 patients underwent total thyroidectomy for a variety of thyroid gland disorders. They were divided into two groups; 97 patients in Group A had parathyroid glands preserved in situ, while 291 patients in Group B had at least one parathyroid gland autotransplanted in ipsilateral sternocleidomastoid muscle. Both groups were followed for six months for the assessment of parathyroid function. Fisher's exact test was used for comparison between the two groups. **Results:** The mean age of Group A was 42.46±15.30 years, while in Group B it was 39.16±18.91 years. Overall male-to-female ratio was 1:3.5. In Group A, 3 (3.09%) patients developed permanent hypocalcaemia while in Group B only 1 (0.34%) patient developed permanent hypocalcaemia. **Conclusion:** Autotransplantation of at least one parathyroid gland after total thyroidectomy is a procedure with predictable outcome associated with minimal risk of permanent hypoparathyroidism.*

Keywords: Parathyroid autotransplantation, Total thyroidectomy

1. Introduction

Total thyroidectomy has become the preferred treatment option for a variety of thyroid disorders.¹⁻³ Post-operative hypocalcaemia is a recognised complication of thyroid surgery. Although most of the patients recover, yet permanent hypoparathyroidism ranges from 1-32% of patients undergoing thyroid surgery.^{4, 5} Parathyroid gland injury can result from inadvertent removal, interruption of blood supply and haematoma formation. To prevent this, meticulous dissection of the precarious blood supply of the glands, intracapsular dissection and less radical resection of the thyroid gland short of total thyroidectomy have been used.⁵⁻⁸ However, a technique that reliably preserves parathyroid gland in situ is still lacking.

Parathyroid gland autotransplantation, first described in humans by Lahey⁹ in 1926, remained a forgotten option for almost 50 years when Wells et al reported the first large series of patients receiving parathyroid autografts with confirmed function of the transplanted tissue clinically, physiologically and histological.^{10, 11} Since then autotransplantation of the parathyroid gland has found its way in a variety of thyroid and head and neck surgeries.

Parathyroid gland has been shown to be taken up well by the host tissues and a very predictable outcome can be expected.^{6, 12} This phenomenon has been demonstrated in volunteers who participated in a study to undergo parathyroid excision and re-implantation in the forearm and later evaluated by histology and electron microscopy,

as well as in patients undergoing parathyroidectomy and thyroidectomy.⁸ Keeping in view these facts, it appears that preservation of parathyroid function by autotransplantation has a more predictable outcome compared to the preservation of the glands in situ.

After the adoption of total thyroidectomy as the preferred technique of a variety of generalised thyroid disorders, the current study was designed to compare autotransplantation with the preservation of parathyroid gland in situ regarding parathyroid function.

2. Patients and Methods

The quasi-experimental study was conducted at the Surgical 2 Unit, Krishna Hospital, Karad, India over a period of 11 years, from July 1, 2004 to June 30, 2015. The study design was approved by the Ethical Committee of the hospital. Informed written consent was obtained from all patients. All those patients aged 18 years and above scheduled for total thyroidectomy were included in the study. Patients in whom the operation was converted to subtotal thyroidectomy, patients with pre-operative diagnosed hypocalcaemia due to hypoparathyroidism and patients scheduled for re-do surgery or complete total thyroidectomy were excluded from the study.

A policy of total thyroidectomy was adopted since July 1998 for generalised thyroid pathology such as multinodular goitre, Graves disease and thyroid malignancy requiring removal of the total gland. A total of

388 patients were included in the study. All patients were extensively tested for thyroid function tests and serum calcium levels routinely and for isotope scintigraphy, serum parathyroid hormone (PTH) levels, fine needle aspiration cytology, ultrasonography, X-rays of neck and thoracic inlet and computed tomography (CT) scans wherever indicated. All the patients were scheduled for total thyroidectomy on the next available list. All surgeries were performed by a single surgeon. For the preservation of parathyroid function, two strategies were adopted; either to preserve the glands in situ or to autotransplant at least one parathyroid gland in the ipsilateral sternocleidomastoid muscle, and, accordingly, the patients were divided into two groups. Group A included the patients in whom all the parathyroid glands were preserved in situ, and Group B had patients in whom at least one parathyroid gland was auto-transplanted and the remaining glands preserved in situ. Initially, patients were randomly assorted into the two groups, but after seeing favourable results with autotransplantation, a routine policy of autotransplantation was adopted. Thus, Group A included 97 patients and Group B included 291 patients.

The operative strategy for Group A consisted of visually identifying the parathyroid glands in situ, intracapsular dissection of the thyroid gland and avoidance of ligation of the inferior thyroid artery and after visual inspection of the thyroid gland, if any parathyroid gland was removed inadvertently, it was taken for autotransplantation, and the respective patient was excluded from the group.

Group B, after or during the removal of the thyroid specimen, the surface of the thyroid gland and the area of the thyroid bed was visually inspected and one parathyroid gland was identified, removed, preserved in cold saline slush and divided into mm-thick pieces with the help of surgical blade. An avascular pocket was created in sternocleidomastoid muscle and the pieces of parathyroid glands were implanted, and the muscle pocket was closed with a suture.

After undergoing total thyroidectomy, all the patients were routinely prescribed oral calcium supplements and vitamin D supplements for four weeks. All the patients were followed up at 6-week, 12-week and 6month intervals. At each follow-up visit, serum calcium was measured and, if it was found low, serum PTH levels were determined. Permanent hypocalcaemia was diagnosed when serum calcium (corrected) was less than 9mg/dl with undetectable levels of serum PTH 6 months after surgery. Permanent hypocalcaemia meant failure of the procedure to preserve parathyroid function. Analysis of the data was done and both groups were compared for the frequency of permanent hypocalcaemia. Fischer's exact test was used for comparison and $p < 0.05$ was considered significant.

3. Results

Of the 388 patients, 97 (25%) underwent preservation of parathyroid glands in situ, and 291 (75%) underwent parathyroid autotransplantation of at least one gland. The demographics of both the groups were fairly the same. The mean age for Group A was 42.46 ± 15.30 years and for

Group B, 39.16 ± 18.91 years. Male-to-female ratio was 1:3.5; in Group A it was 1:3.6, and in Group B it was 1:3.4.

The commonest indication for total thyroidectomy in both the groups was Euthyroid multinodular goitre (MNG), followed by toxic multinodular goitre, Graves disease and malignancy (Table-1). After the removal of the thyroid gland and careful inspection of the specimen, accidentally removed number of parathyroid glands along with the thyroid gland included; the removal of single gland in 52 (53.6%) cases; two in 19 (19.58%) and three in 6 (6.18%) cases. In Group B, single-gland transplantation was done in 203 (69.5%) patients; two glands in 57 (19.5%); and three glands in 29 (9.9%). Post-operative stay in Group A was 1.9 ± 1.64 days (range 1-13 days) and in Group B it was 1.8 ± 1.56 days (ranges 1-11 days).

The frequency of transient hypocalcaemia in post-operative cases, defined as symptomatic hypocalcaemia.

Table 1: Indications of total thyroidectomy

	Group A n(%)	Group B n(%)	P value*
Euthyroid Multinodular Goitre	59(60.82)	179(61.51)	0.90
Toxic Multinodular Goitre	23(23.71)	61(20.96)	0.57
Graves Disease	11(11.34)	29(9.96)	0.70
Malignancy	04(4.12)	22(7.56)	0.35
Total	97(100)	291(100)	

*Calculated with Fischer's exact test
 Value ≥ 0.05 is considered as significant difference

Table 2: Frequency of hypocalcaemia

	Group A n=97	Group B n=291	P value†
Temporary hypocalcaemia	17(16.8)	69(23.7)	0.2586
Permanent hypocalcaemia	3(2.9)	1(0.3)	0.0417

†Two sided p value calculated with Fisher's exact test. $p < 0.05$ means significant difference between the two groups
 Numbers in parenthesis denote percent

Within the first 6 months after surgery, was in 17 (16.8%) cases in Group A, and in 69 (23.7%) cases in Group B (Table-2). Here the difference in both the groups was not statistically significant. The most important result was the frequency of permanent hypocalcaemia, which in Group A accounted for 3 (2.9%) cases, and 1 (0.3%) in Group B. The difference was statistically significant.

4. Discussion

Since the adoption of routine total thyroidectomy for a variety of thyroid gland disorders, preservation of parathyroid gland function has been one of the prime concerns. The results of our study show that auto-transplantation of at least one parathyroid gland during the course of total thyroidectomy results in minimal risk of permanent hypoparathyroidism. Previously, one of the

reasons for advocating subtotal thyroidectomy was to ensure that the blood supply to the parathyroid glands remained intact and that the risk of permanent hypocalcaemia was eliminated.

Total thyroidectomy from a historical perspective has been fraught with certain dangers. It was Theodore Kocher, the pioneer of thyroid surgery, who initially was an advocate of total thyroidectomy, but later abandoned the procedure in favour of subtotal thyroidectomy because his patients suffered from a condition described by him as 'strumipriva'. His patients were probably suffering from hypothyroidism. This practice of subtotal thyroidectomy continued for almost the next century until it was recognised that leaving a remnant of the thyroid gland resulted in long-term problems.¹³

Several problems have been identified to arise from the remnant in subtotal thyroidectomy e.g. recurrence in excised MNG and the development of carcinoma in the remnant, and recurrence of hyperthyroidism in Graves disease in a significant number of patients.^{2, 14} Another point of concern has been that for any recurrent problem of the gland, redo surgery is fraught with complications and associated with definite morbidity to the patient.^{1, 2}

These facts encouraged thyroid surgeons to rethink about the bygone procedure of total thyroidectomy as a more favoured option for malignant as well as benign diseases of the thyroid gland.

Today total thyroidectomy has become the preferred operation for a variety of thyroid disorders. Wheeler commented in editorial in the Lancet, "Total thyroidectomy for benign thyroid disease is likely to become an accepted component of the endocrine surgeon's armamentarium."¹⁵

Parathyroid glands are at risk of being damaged during total thyroidectomy mainly due to inadvertent removal, interruption of the blood supply and haematoma formation.^{4, 16} Careful preservation of the parathyroid glands in situ is the goal, but not always practical and the results have been unpredictable. A normal looking parathyroid gland in situ may not function post-operatively. For this reason, thyroid surgeons adopted the technique of autotransplantation.

There are two schools of thought; one advocates selective autotransplantation while the other favours routine autotransplantation. Selective autotransplantation means that parathyroid glands should be auto-transplanted whenever the viability of the gland in situ is in question. In this approach, the surgeon usually has a false sense of security that the blood supply is adequate, which in reality is not, but with the evolution of surgical techniques and adoption of intracapsular dissection, the results have improved. Routine autotransplantation means that at least one parathyroid gland be removed and auto-transplanted.^{17, 18} Our study favours the latter approach.

In routine autotransplantation, even if there is damage to the rest of the glands, the transplanted gland will resume function within a few weeks. During this time, the patient may undergo a period of transient hypocalcaemia, but in the long term, as the transplanted gland regains function, the risk of permanent hypoparathyroidism is practically abolished. During this lag period, the patient is advised to take calcium and vitamin D supplements. In our study, the patients were routinely prescribed these supplements.^{19, 20}

A careful search of the literature reveals that transplantation of at least one gland has a more predictable outcome compared to leaving all glands in situ. Due to this fact, leading centres of thyroid surgery throughout the world have started the policy of more frequent total thyroidectomy and routine autotransplantation of at least one parathyroid gland.^{1, 3, 7, 16} It will increase the risk of hypocalcaemia in the short term, but has in theory the potential to reduce the incidence of iatrogenic permanent hypoparathyroidism to zero.¹⁸

5. Conclusion

Routine autotransplantation of parathyroid glands is the preferred procedure to ensure good parathyroid function. At least one in the course of total thyroidectomy is recommended as the outcome gets more predictable.

References

- [1] Sakorafas GH, Stafyla V, Bramis C, Kotsifopoulos N, Kolettis T, Kassaras G. Incidental parathyroidectomy during thyroid surgery: An underappreciated complication of thyroidectomy. *World J Surg* 2005; 29: 1539-43
- [2] Lo CY. Parathyroid auto transplantation during thyroid surgery. *ANZ J Surg* 2002; 72: 902-7
- [3] Conti Freitas LC, Foss Freitas MC, Lucca LJ, Costa JAC, Mamede RC, Foss MC. Dynamics of parathyroid hormone secretion after total parathyroidectomy and auto transplantation. *World J Surg* 2009; 33: 1403-7
- [4] Abboud B, Sleilaty G, Braidy C, Zeineddine S, Ghorra C, Abadjian G, et al. Careful examination of thyroid specimen intraoperatively to reduce incidence of inadvertent parathyroidectomy during thyroid surgery. *Arch Otolaryngol Head Neck Surg* 2007; 133:1105-10
- [5] El-Sharaky MI, Kahlil MR, Sharaky O, Sakr MF, Fadaly GA, El-Hammadi HA, et al. Assessment of parathyroid autransplantation for preservation of parathyroid function after total thyroidectomy. *Head Neck* 2003; 25: 799-807
- [6] Lahey FH. The transplantation of parathyroids in partial thyroidectomy. *Surg Gynecol Obstet* 1926; 62: 508-9
- [7] Wells SA Jr, Stirman JA Jr, Bolman RM 3rd. Parathyroid transplantation. *World J Surg* 1977; 1: 747-56
- [8] Olson JA Jr, DeBenedetti MK, Baumann DS, Wells SA Jr. Parathyroid autotransplantation during thyroid surgery. Results of long term follow-up. *Ann Surg* 1996; 223: 472-8

- [9] Lo CY, Lam KY. Postoperative hypocalcaemia in patients who did or did not undergo parathyroid autotransplantation during thyroidectomy: a comparative study. *Surgery* 1998; 124: 1081-7
- [10] Welbourn RB. The Thyroid. In: Welbourn RB (ed.) *The History of Endocrine Surgery*. New York: Praeger, 1990; 19-88
- [11] Amanda D, Ana G, Tom SR, Bruce R, Leigh D. Progressive increase in thyroid dysfunction after subtotal thyroidectomy for Graves disease. *Asian J Surg* 2000; 23: 131-5
- [12] Wheeler MH. Total thyroidectomy for benign thyroid disease. *Lancet* 1998; 351: 1526-7
- [13] Lo CY, Tam SC. Parathyroid autotransplantation during thyroidectomy: documentation of graft function. *Arch Surg* 2001; 136: 1381-5
- [14] Gauger PG, Reeve TS, Wilkinson M, Delbridge LW. Routine parathyroid autotransplantation during total thyroidectomy: the influence of technique. *Eur J Surg* 2000; 166: 605-9
- [15] Zedenius J, Wadstrom C, Delbridge L. Routine autotransplantation of at least one parathyroid gland during total thyroidectomy may reduce permanent hypoparathyroidism to zero. *Aust NZ J Surg* 1999; 69: 794-7
- [16] Roh JL, Park CI. Routine oral calcium and vitamin D supplements for prevention of hypocalcaemia after total thyroidectomy. *Am J Surg* 2006; 192: 675-8
- [17] Moore FD Jr. Oral calcium supplements to enhance early hospital discharge after bilateral surgical treatment of the thyroid gland or exploration of the parathyroid glands. *J Am Coll Surg* 1994; 178: 11-6