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Original Research Article

The number of parathyroid glands preserved during thyroidectomy and relationship between hypoparathyroidism

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ABSTRACT

Background: The aim of the study was to determine the number of parathyroid glands that need to be preserved to prevent hypoparathyroidism and to understand the relation between the number of parathyroid glands preserved and hypoparathyroidism.
Methods: A retrospective study was performed on 350 patients who had undergone trans cervical total thyroidectomy with or without neck dissection for papillary thyroid carcinoma between July 2010 to August 2015.
Results: Incidental parathyroidectomy occurred in 19.1% of patients, one parathyroid gland in 17.8%, two in 2% and 3 in 0.5%. Transient hypoparathyroidism increased when incidental parathyroidectomy occurred on multivariate regression analysis, but it was not influenced by the actual number of parathyroid glands removed. There was no relationship between the number of parathyroid glands preserved and hypoparathyroidism.
Conclusions: It is not compulsorily required to prevent permanent hypoparathyroidism, but the preservation of all the four parathyroid glands during thyroidectomy decreases the incidence of transient hypoparathyroidism. When auto transplantation is not performed, to prevent permanent hypoparathyroidism, preserving at least one parathyroid gland with an intact blood supply is sufficient.

Keywords: Hypoparathyroidism, Parathyroid, Thyroidectomy

INTRODUCTION

A major complication of thyroidectomy is hypoparathyroidism. About 10 to 46% of the incidence of transient hypoparathyroidism after thyroidectomy is reported where as permanent hypoparathyroidism is as low as zero and as high as 43%.[1] The use of medication and biochemical tests is increased by postoperative hypoparathyroidism and hospital stay is prolonged thus adding to the overall cost of thyroidectomy.[2,3,4] The key to minimizing hypoparathyroidism following thyroidectomy is preserving the parathyroid gland and its blood supply. However, the relationship between the hypoparathyroidism and the number of parathyroid glands preserved is not well understood. The aim of the study was to evaluate the clinical characteristics and the frequency of hypoparathyroidism according to the number of parathyroid glands preserved during thyroidectomy and to estimate the minimum number of parathyroid glands that need to be preserved to prevent hypoparathyroidism.

METHODS

A retrospective study was performed on 350 patients who had undergone trans cervical total thyroidectomy with or without neck dissection for papillary thyroid carcinoma between July 2010 to August 2015. 50 patients were

excluded who had undergone parathyroid gland auto transplantation. Patients who had severe chronic renal insufficiency, preoperative alterations of parathyroid function, and who had severe chronic renal insufficiency, or those patients who had diseases that interfered with haemostasis of calcium, and those patients who had undergone robotic or endoscopic thyroidectomy, or completion or revision thyroidectomy were excluded from the study. The patient and tumor characteristics, extent of central and lateral neck dissection, number of para- thyroid glands preserved, number found incidentally in the surgical specimens, the need for administration of intravenous calcium supplements, hypoparathyroidism, and other surgical complications were analysed. The operative procedure included identification of the parathyroid glands and capsular dissection so that the parathyroid glands are preserved and its vasculature during the central neck dissection (CND). The parathyroid glands were preserved with its blood supply from the inferior thyroid artery and its branches. We identified all superior parathyroid glands, and inferior parathyroid glands were identified in cases when CND was needed. It was autotransplanted to the ipsilateral sternocleidomastoid muscle only when devascularization of the parathyroid gland was evident, and when it was performed after confirmation by frozen section. Therefore, we excluded cases with auto-transplantation to reduce bias. As, it is not always possible to identify all the parathyroid glands during thyroidectomy, the number of parathyroid glands preserved was obtained by subtracting the number of parathyroid glands in a given specimen from four. As iPTH has a short biological half-life, parathyroid function was measured as intact parathyroid hormone (iPTH), so it was used as an index of parathyroid gland function. Intact PTH was estimated by the electro chemiluminescence immunoassay (ECLIA) on Elecsys immunoassay analyser. Baseline levels of iPTH, total calcium (Ca), and ionized Ca were evaluated preoperatively, and their postoperative levels were measured after 24 hours after skin closure, 1 week, and 6 months, and when necessary. The decreased ratio of iPTH was calculated as: (preoperative iPTH-postoperative iPTH) ×100/preoperative iPTH.

Hypoparathyroidism was defined as any drop in serum iPTH below the normal limit (normal range, 15 to 65 pg/mL), regardless of hypocalcemic symptoms. Permanent hypoparathyroidism was defined as lack of recovery of the iPTH to the normal range within six months.[1,8-10] Hypocalcemia was defined as decreased total calcium level (normal range, 8.4 to 10.4 mg/dl) or decreased ionized calcium level (normal range, 1.13 to 1.32 mmol/L) regardless of symptoms. All patients were followed up for at least six months after surgery.

RESULTS

Table 1 shows the male patients were 70 (20%) and female patients were 280 (80%) who were ranging from 16 to 80 years, with a mean age of 50.9. The tumor characteristics associated with the number of excised parathyroid glands which included tumor size was 11.2±8.7, tumor multiplicity was 96, tumor bilaterality was 97. Tumor was located mostly in the right, followed by left, bilateral and confined to isthmus.

Table 1: Patient and tumour characteristics associated with the number of excised parathyroid glands.

Variable		A-N = 280,0	B-N = 61,1	C-N = 9, 2 or more	Total, n = 350
Age		51.1±11.6	52.8±14.7	47.2±5.98	50.9±11.4
Gender	Males	51 (18.2%)	16 (26.2%)	3 (33.3%)	70 (20%)
	Females	229 (81.7%)	45 (73.7%)	6 (66.6%)	280 (80%)
Tumor size		11.9±8.7	12.0±6.5	13.4±10.1	11.2±8.7
Tumor multiplicity		70/280 (25%)	24/61 (39.3%)	2/9 (22.2%)	96/350 (27.4%)
Tumor bilaterality		56/280 (20%)	41/61 (67%)	-	97/350 (27.7%)
Tumor location					
Right		101 (36.07%)	15 (24.6%)	4 (44.4%)	120 (34.28%)
Left		78 (27.9%)	27 (44.26%)	5 (55.5%)	110 (31.42%)
Bilateral		90 (32.1%)	15 (24.6%)	-	105 (30%)
Confined toisthmus		11 (3.92%)	4 (6.55%)	0	15 (4.28%)

N is number of parathyroid glands in resected specimen.

There was no difference observed in patient and tumor characteristics, TNM stage, extrathyroidal extension and complication of surgery with or without transient hypoparathyroidism. Only incidental parathyroid was identified as independent risk factor for transient hypoparathyroidism, in multivariate logistic regression analysis. There was no relation between the number of preserved parathyroid glands and permanent hypoparathyroidism. There was a decrease observed in all the days i.e. from 24 hours, 1 week and 6 months in all the groups i.e. A, B and C.

Table 2: T and N classification.

Variable	A-N=280,0	B-N=61,1	C-N=9, 2 or more	Total, n=350
T Classification				
T1	114 (40.7%)	15 (24.6%)	3 (33.3%)	132 (37.7%)
T2	71 (25.4%)	19 (31.14%)	4 (44.4%)	94 (26.9%)
T3	85 (30.4%)	23 (37.7%)	1 (11.1%)	109 (31.1%)
T4	10 (3.6%)	4 (6.6%)	1 (11.1%)	15 (4.3%)
N classification				
N0	175 (62.5%)	25 (41%)	2 (22.2%)	202 (57.7%)
N1	105 (37.5%)	36 (59%)	7 (77.7%)	148 (42.3%)

Table 3: Shows TNM stage.

Variable	A-N=280,0	B-N=61,1	C-N=9, 2 or more	Total, n=350
TNM Classification				
I	126 (45%)	19 (31.1%)	3 (33.3%)	148 (42.3%)
II	12 (4.3%)	1 (1.6%)	0 (0.0%)	13 (3.7%)
III	93 (33.2%)	20 (32.8%)	4 (44.4%)	117 (33.5%)
IV	49 (17.5%)	21 (34.4%)	2 (22.2%)	72 (20.5%)
Extrathyroidal	145/280	40/61	6/9	191/350

Table 4: Surgical extent and complications associated with the number of excised parathyroid glands.

Variable	A-N=280,0	B-N=61,1	C-N=9, 2 or more	Total, n=350
CND				
None	95 (33.9%)	5 (8.2%)	0 (0.0%)	100 (28.6%)
Unilateral	82 (29.3%)	26 (42.6%)	1 (11.1%)	109 (31.1%)
Bilateral	103 (36.8%)	30 (49.2%)	8 (88.8%)	141 (40.3%)
Retrieved CLN (No)	5.0±6.3	7.2±5.0	7.8±2.2	5.7±5.0
Metastatic CLN (No)	1.3±2.8	2.5±3.5	2.4±2.9	1.2±3.6
Lateral ND	55/280 (19.6%)	20/61 (32.8%)	1/9 (11.1%)	76/350 (21.7%)
Operation time	150.3±63.2	165.0±94.2	195.0±150.2	163.0±75.2
Hypoparathyroidism				
Temporary	170/280 (60.7%)	40/61 (65.6%)	6/9 (66.6%)	216/350 (61.7%)
Permanent	11/280 (3.9%)	5/61 (8.2%)	1/9 (11.1%)	17/350 (4.9%)
IV Calcium administration	32/280 (11.4%)	9/61 (14.8%)	2/9 (22.2%)	43/350 (12.3%)
Vocal cord paralysis				
None	272/280	58/61	7/9	337/350
Temporary	7/280	3/61	2/9	12/350
Permanent	1/280	0/61	0/9	1/350
Haematoma	10/280	3/61	0/9	13/350

DISCUSSION

Many studies have reported which has shown the number of parathyroid glands preserved during thyroidectomy and relationship between hypoparathyroidism. Song CM et al, analysed 454 patients who underwent total thyroidectomy for papillary thyroid carcinoma.[5] We analyzed the frequency of hypoparathyroidism according to the number of parathyroid glands preserved. Incidental parathyroidectomy occurred in 19.8% of the patients; one parathyroid gland in 17.6%, two in 1.5%, and three in 0.7%. Transient hypoparathyroidism was increased when incidental parathyroidectomy occurred (odds ratio 1.83, 95% confidence interval 1.04 to 3.23, P = 0.036) on multivariate regression analysis, but was not influenced by the actual number of parathyroid glands removed. There was no relationship between the number of parathyroid glands preserved and permanent hypoparathyroidism (P = 0.147). Preservation of all parathyroid glands decreases transient hypoparathyroidism compared with when three or fewer glands are preserved, but does not affect permanent hypoparathyroidism. During total thyroidectomy, preserving at least one parathyroid gland with an intact blood supply appears to be sufficient to prevent permanent hypoparathyroidism when autotransplantation

is not performed. Palazzo FF et al, conducted a study in which parathyroid autotransplantation is a technique for ensuring the continued function of parathyroid tissue at the time of total thyroidectomy (TT).[6] The aim of this study was to ascertain whether the number of parathyroid 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. Cavicchi O et al, conducted a study whose purpose was to identify the risk factors for postoperative transient hypoparathyroidism in a group of patients undergoing thyroid surgery.[7] A prospective study was conducted on 604 patients undergoing thyroid surgery. Gender, final diagnosis, extent of resection, biology of pathology, intrathoracic involvement, surgery for recurrent multinodular goiter, and presence and number of parathyroid glands in a surgical specimen were analyzed as risk factors for postoperative transient hypoparathyroidism. The chi-square test and a logistic regression analysis were applied. On logistic regression analysis, only the extent of surgery constituted an independent variable for transient hypo-parathyroidism (P=0.001). The extent of surgery to central and/or lateral neck lymph nodes is responsible for a high rate of transient hypoparathyroidism owing to a high probability of unplanned parathyroidectomy or parathyroid gland devascularization. Sasson AR et al, conducted a retrospective study at tertiary referral cancer center to identify any risk factors for incidental parathyroidectomy and to define its association with symptomatic postoperative hypocalcemia.[8] Consecutive patients who underwent thyroid surgery between 1991 and 1999. Patients who underwent procedures for locally advanced thyroid cancer requiring laryngectomy, tracheal resection, or esophagectomy were excluded. All pathology reports were reviewed for the presence of any parathyroid tissue in the resected specimen. Slides were reviewed, and information regarding patient demographics, diagnosis, operative details, and postoperative complications was collected. The main outcome measure was identification of parathyroid tissue in resected specimens and postoperative symptomatic hypocalcemia. A total of 141 thyroid procedures were performed: 69 total thyroidectomies (49%) and 72 total thyroid lobectomies (51%). The findings were benign in 68 cases (48%) and malignant in 73 cases (52%). In the entire series, incidental parathyroidectomy was found in 21 cases (15%). Parathyroid tissue was found in intrathyroidal (50%), extracapsular (31%), and central node compartment (19%) sites. The performance of a concomitant modified radical neck dissection was associated with an increased risk of unplanned parathyroidectomy (P =0.05). There was no association of incidental parathyroidectomy with postoperative hypocalcemia (P =0.99). Multivariate analysis identified total thyroidectomy as a risk factor for postoperative hypocalcemia (P =0.008). In the entire study group, transient symptomatic hypocalcemia occurred in 9 patients (6%), and permanent hypocalcemia occurred in 1 patient who underwent a total thyroidectomy and concomitant neck dissection. Unintended parathyroidectomy, although not uncommon, is not associated with symptomatic postoperative hypocalcemia. Modified radical neck dissection may increase the risk of incidental parathyroidectomy. Most of the glands removed were intrathyroidal, so changes in surgical technique are unlikely to markedly reduce this risk. Thomusch O et al, conducted a study between January 1 and December 31, 1998, bilateral thyroid surgery was performed on 5846 patients for benign and malignant thyroid disease.[9] Data were prospectively collected by questionnaires from 45 hospitals. A logistic regression model was used to determine independent risk factors. The overall incidence of transient and permanent hypoparathyroidism was 7.3% and 1.5%, respectively. On logistic regression analysis, total thyroidectomy (odds ratio [OR], 4.7), female gender (OR, 1.9), Graves' disease (OR, 1.9), recurrent goiter (OR, 1.7), and bilateral central ligation of the inferior thyroid artery (OR, 1.7) constituted independent risk factors for transient hypoparathyroidism. When the multivariate analysis was confined to permanent hypoparathyroidism, total thyroidectomy (OR, 11.4), bilateral central (OR, 5.0) and peripheral (OR, 2.0) ligation of the inferior thyroid artery, identification and preservation of no or only a single parathyroid gland (OR, 4.1), and Graves' disease (OR, 2.4) emerged as independent risk factors.

Extent of resection and surgical technique had a greater impact on the rates of permanent postoperative hypoparathyroidism than thyroid pathologic condition. In bilateral thyroid surgery, peripheral ligation of the inferior thyroid artery at the thyroid capsule should be favored over central ligation, and at least 2 parathyroid glands should be identified and preserved. High-risk procedures, such as total thyroidectomy and Graves' disease, require special surgical training and expertise.

Almquist M et al, conducted a study in which permanent hypoparathyroidism, defined as continuing need for vitamin D medication at 1-year post-operatively, was investigated in patients after total thyroidectomy.[10] Blood levels of calcium and parathyroid hormone (PTH) were measured intra-operatively, the day after surgery and at 1 month post-operatively. Logistic regression analysis was performed to investigate the risk of vitamin D treatment at last follow-up, calculated as odds ratios (ORs) with 95% confidence intervals (CIs). Patients were followed until cessation of vitamin D and/or calcium medication, until death, loss to follow-up, or end of follow-up, whichever came first. A total of 519 patients were included. The median (range) follow-up in patients unable to cease vitamin D was 2.7 (1.2-10.3) years. The rate of permanent hypoparathyroidism was 10/519, 1.9%. Parathyroid auto-transplantation was performed in 90/519 (17.3%) patients. None of these developed permanent hypoparathyroidism, nor did any patient with normal PTH day 1 (>1.6 pmol/l or 15 pg/ml). The adjusted risk (OR, 95% CI) for permanent hypoparathyroidism for log PTH on day 1 was 0.25 (0.13-0.50). In patients not auto-transplanted and with unmeasurable PTH day 1 (<0.7 pmol/l or 6.6 pg/ml), 8/42 (19.2%) developed permanent hypoparathyroidism. Auto-transplantation protects against permanent hypoparathyroidism, whereas low PTH day 1 is associated with high risk.

CONCLUSION

It can be concluded that it's not compulsorily required to prevent permanent hypoparathyroidism, but the preservation of all the four parathyroid glands during thyroidectomy decreases the incidence of transient hypoparathyroidism. When autotransplantation is not performed, to prevent permanent hypoparathyroidism, preserving at least one parathyroid gland with an intact blood supply is sufficient.

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REFERENCES

1. Pattou F, Combemale F, Fabre S, Carnaille B, Decoulx M, Wemeau JL, et al. Hypocalcemia following thyroid surgery: incidence and prediction of outcome. World J Surg. 1998;22:718-24.
2. Shaha AR, Jaffe BM. Parathyroid preservation during thyroid surgery. Am J Otolaryngol. 1998;19:113-7.
3. McHenry CR, Speroff T, Wentworth D, Murphy T. Risk factors for postthyroidectomy hypocalcemia. Surg. 1994;116:641-7.
4. Lappas D, Noussios G, Anagnostis P, Adamidou F, Chatzigeorgiou A, Skandalakis P. Location, number and morphology of parathyroid glands: results from a large anatomical series. Anat Sci Int. 2012;87:160-4.
5. Song CM, Jung JH, Ji YB, Min HJ, Ahn YH, Tae K. Relationship between hypoparathyroidism and the number of parathyroid glands preserved during thyroidectomy. World J Surg Oncol. 2014;12:200.
6. Palazzo FF, Sywak MS, Sidhu SB, Barraclough BH, Delbridge LW. Parathyroid autotransplantation during total thyroidectomy: does the number of glands transplanted affect outcome? World J Surg. 2005;29:629-31.
7. Cavicchi O, Piccin O, Caliceti U, Decataldis A, Pasquali R, Ceroni A. Transient hypoparathyroidism following thyroidectomy: a prospective study and multivariate analysis of 604 consecutive patients. Otolaryngol Head Neck Surg. 2007;137:654-8.
8. Sasson AR, Pingpank JF Jr, Wetherington RW, Hanlon AL, Ridge JA. Incidental parathyroidectomy during thyroid surgery does not cause transient symptomatic hypocalcemia. Arch Otolaryngol Head Neck Surg. 2001;127:304-8.
9. Thomusch O, Machens A, Sekulla C, Ukkat J, Brauckhoff M, Dralle H. The impact of surgical technique on postoperative hypoparathyroidism in bilateral thyroid surgery: a multivariate analysis of 5846 consecutive patients. Surg. 2003;133:180-5.
10. Almquist M, Hallgrimsson P, Nordenström E, Bergenfelz A. Prediction of permanent hypoparathyroidism after total thyroidectomy. World J Surg. 2014;38(10):2613-20.

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