

ORIGINAL ARTICLE

Impact of preserving the parathyroid glands on hypocalcemia after total thyroidectomy with neck dissection

Yon Seon Kim

Department of Surgery, Ulsan University Hospital, University of Ulsan College of Medicine, Ulsan, Korea

Purpose: The aims of this study were to determine the incidence and evaluate the risk factors for hypocalcemia after total thyroidectomy and to investigate how many parathyroid glands should be preserved to prevent postoperative hypocalcemia. **Methods:** From March 2007 to February 2011, a retrospective review of 866 patients who underwent total thyroidectomy and node dissection for thyroid cancer was performed. The incidence and predisposing factors for hypocalcemia were analyzed. Among them, a total of 191 cases had four of their parathyroid glands identified intraoperatively. These patients were then divided into one preserved parathyroid gland group (group I, n = 22) and two or more preserved parathyroid glands group (group II, n = 169). The incidence of hypocalcemia with regards to the number of preserved parathyroid glands was determined and the results between the two groups were compared. The total calcium, ionized calcium and parathyroid hormone levels were compared between the two groups. **Results:** The overall incidence of transient and permanent hypocalcemia was 9.2% and 0.5%, respectively. The decreased number of preserved parathyroid gland and increased number of removed central lymph node were the significant risk factors for developing postoperative hypocalcemia. In 191 cases identified with four parathyroid glands, the incidence of hypocalcemia was related to the number of preserved glands (group I, 22.7%; group II, 3.0%; $P < 0.001$). **Conclusion:** The insufficient number of preserved parathyroid glands is the only cause of hypocalcemia after total thyroidectomy and node dissection. At least one preserved parathyroid gland may prevent postoperative permanent hypocalcemia.

Key Words: Thyroid neoplasms, Thyroidectomy, Hypocalcemia, Parathyroid glands

INTRODUCTION

Postthyroidectomy hypocalcemia is a common complication after thyroidectomy, although thyroidectomy is still a safe procedure. It is usually transient but some cases can become permanent due to loss of functioning para-

thyroid gland. This can cause significant discomfort in affected patients who will eventually need to take oral calcium and vitamin D for a long time [1]. The possible causes of hypocalcemia are injury to the parathyroid glands or its blood supply, extensive resection, neck dissection with total thyroidectomy, Graves' disease, carcinoma, and hemo-

Received March 29, 2012, Revised May 16, 2012, Accepted June 4, 2012

Correspondence to: Yon Seon Kim

Department of Surgery, Ulsan University Hospital, University of Ulsan College of Medicine, 877 Bangeojinsunhwan-doro, Dong-gu, Ulsan 682-714, Korea

Tel: +82-52-250-7109, Fax: +82-52-250-7350, E-mail: drsun@korea.com

© Journal of the Korean Surgical Society is an Open Access Journal. All articles are distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/3.0/>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

dilution [2-7]. Among them, parathyroid gland injury is the most common factor for developing hypocalcemia. To minimize parathyroid injury, an attempt to look for all the parathyroid glands and preserved their blood supply should be made during the operation. However, it is difficult to find all parathyroid glands and to preserve these identified parathyroid glands due to the high probability of inflicting damage to their blood supply during the search process and dissection. Also, the extent of thyroidectomy and node dissection increases the likelihood of damaging the blood supply of the parathyroid glands [2,3]. Many reports have stated that parathyroid auto-transplantation can reduce the incidence of hypocalcemia, when unintentionally removed or devascularized parathyroid glands were found during operation [8,9]. Sometimes, parathyroid glands may be found within the postoperative specimen, when it was unknowingly removed with the thyroid or lymph node during the operation [10]. It is interesting to know how many parathyroid glands should be preserved *in situ* in order to prevent postoperative hypocalcemia. The aims of this study were to determine the incidence of and to evaluate the risk factors for hypocalcemia after total thyroidectomy and node dissection for thyroid cancer; to investigate the incidence of hypocalcemia according to the number of preserved parathyroid glands; and to investigate how many parathyroid glands should be preserved to prevent postoperative hypocalcemia.

METHODS

Eight hundred sixty-six patients, who underwent total thyroidectomy and node dissection for thyroid cancer at the surgical department of the present hospital between March 2007 and February 2011, were retrospectively reviewed. The patients consisted of 115 men and 751 women. The mean age was 46.3 years old (range, 15 to 78 years old). The preoperative diagnoses were papillary thyroid carcinoma in 856 patients, follicular carcinoma in 6, medullary thyroid carcinoma in 2, and undifferentiated carcinoma in 2. The median size of the primary tumor was 11 mm (range, 2 to 70 mm). Before surgery, 21 patients

were treated for Grave's disease. In all patients, total thyroidectomy and central cervical lymph node dissection were performed. In 75 patients, lateral neck dissection was performed at the same time, because lymph node metastases were suspected on the basis of a preoperative ultrasound examination and ultrasound guided fine needle aspiration. Lateral neck lymph node metastases were confirmed in 66 of them. The demographic data are summar-

Table 1. Clinicopathologic characteristics of the patients

Characteristic	Value
Sex	
Male	115 (13.3)
Female	751 (86.7)
Age (yr)	46.27 ± 11.03 (15-78)
<45	401 (46.3)
≥45	465 (53.7)
Presence of Graves' disease	21 (2.4)
Operation	
Total thyroidectomy + CLND	791 (91.3)
Total thyroidectomy + MRND	75 (8.7)
Diagnosis	
Papillary thyroid cancer	856 (98.8)
Follicular thyroid cancer	6 (0.7)
Medullary thyroid cancer	2 (0.2)
Undifferentiated thyroid cancer	2 (0.2)
Mass size (cm)	1.08 ± 0.82 (0.2-7)
Multifocality	
Single	573 (66.2)
Multiple (≥2)	293 (33.8)
Extrathyroid extension	
No	330 (38.1)
Yes	536 (61.9)
Thyroiditis	
No	660 (76.2)
Yes	206 (23.8)
Removed central lymph node	10.96 ± 6.21 (1-53)
No. of preserved parathyroid glands	1.65 ± 1.01 (0-4)
T stage	
T1	314 (36.3)
T2	14 (1.6)
T3	471 (54.4)
T4a	63 (7.3)
T4b	4 (0.5)
N stage	
No	432 (49.9)
N1a	368 (42.5)
N1b	66 (7.6)

Values are presented as mean ± SD (range) or number (%). CLND, central lymph node dissection; MRND, modified radical neck dissection.

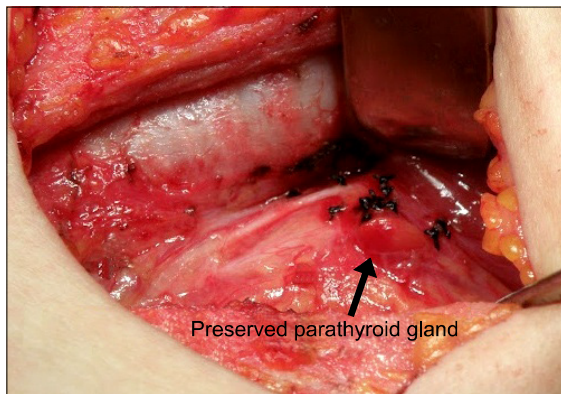


Fig. 1. Preserved parathyroid gland with intact blood supply.

ized in Table 1.

The standard initial surgical procedure done was extracapsular thyroidectomy and meticulous trachea-esophageal groove dissection. During the operation, all attempts were made to identify all the parathyroid glands and preserve their blood supply [2,11]. If it was necessary to remove the parathyroid gland due to its proximity to the cancer or its unintentional devascularization, the removed parathyroid gland was immediately autotransplanted into the sternocleidomastoid muscle. The handling of the parathyroid glands during operation were described into 5 types. The preserved type was defined as identifying a grossly tan parathyroid gland with intact blood supply after the operation (Fig. 1). The color changed type was defined as parathyroid gland looking grossly congested and was judged as having low chance of survival. The autotransplantation type was defined as isolated parathyroid gland being implanting into the sternocleidomastoid muscle due to inadvertent gland removal, accidentally severing the parathyroid gland's blood supply during surgery or the gland was located in the anterior portion of the thyroid lobe and was receiving its blood supply from the thyroid gland [2]. The removed type was defined as parathyroid gland being removed with the thyroid gland due to its proximity to the cancer or was incidentally found within the postoperative specimen. The non-identified type was defined as parathyroid gland not being found during the operation. Successful preservation of the parathyroid glands was considered only for the first type. The remaining four types were considered non-pres-

ervation of the parathyroid glands.

The patients who suffered with numbness as signs of hypocalcemia and patients who had four intraoperatively identified parathyroid glands measured serum calcium, ionized calcium, and intact parathyroid hormone (iPTH) on postoperative days (PODs) 1, 3, and 7 days. Patients who have hypocalcemic symptoms along with total calcium level less than 7.8 mg/dL (normal range, 7.8 to 10.0 mg/dL) or ionized calcium level less than 0.96 mM/L (normal range, 0.96 to 1.40 mM/L) were considered as having hypocalcemia. Patients with hypocalcemia were given oral calcium carbonate 2 g/day and oral 1,25-dihydroxycholecalciferol, 0.5 µg/day. If needed, intravenous calcium gluconate was also administered. Patients who continued to require calcium carbonate and oral 1,25-dihydroxycholecalciferol more than 6 months after the operation were considered as having permanent hypocalcemia. One hundred ninety one patients who had four intraoperatively identified parathyroid glands and without autotransplantation being done on any of the parathyroid glands were divided into three groups. Group I consisted of patients with one parathyroid gland being preserved *in situ*, group II consisted of those with two parathyroid glands preserve *in situ* and group III consisted of those with three or more parathyroid glands preserve *in situ*. The incidence of hypocalcemia in the two groups was compared.

The clinicopathologic characteristics, including patient's sex, age, gender, presence of Graves' disease, multifocality of the lesion, tumor size, extrathyroid extension, thyroiditis, number of identified parathyroid glands, number of preserved parathyroid glands, and number of removed central lymph nodes were investigated. The level of iPTH was measured by electrochemiluminescence immunoassay (Roche, Mannheim, Germany), the normal range being at 15 to 65 pg/mL.

Statistical analyses were performed using the IBM SPSS ver. 18.0 (IBM Co., Armonk, NY, USA). The χ^2 test, t-tests and Fisher's exact test, Mann-Whitney test, and the Logistic regression analyses were used to analyze the variables related to hypocalcemia. The case with a P-value of less than 0.05 was considered to be statistically significant.

RESULTS

During the median follow-up time of 27 months, 80 pa-

Table 2. Clinical features and incidences of complication after total thyroidectomy and lymph node dissection

	No. of patients (%)
Bleeding	2 (0.2)
Hypocalcemia	84 (9.7)
Transient	80 (9.2)
Permanent	4 (0.5)
Hoarseness	11 (1.3)
Chylous fistula	6 (0.7)

tients (9.2%) had transient hypocalcemia and 4 patients (0.5%) had permanent hypocalcemia. The mean number of preserved parathyroid glands was 1.65 ± 1.01 in all patients, 1.75 ± 0.97 among patients with normocalcemia, and 0.71 ± 0.78 among patients with transient hypocalcemia. Other complications such as bleeding, hoarseness, and chylous fistula occurred in 2, 11, and 6 cases, respectively (Table 2). The 80 patients who had transient hypocalcemia, received calcium and 1,25-hydroxyvitamin D supplements for 2 to 4 weeks. All of them recovered with calcium and iPTH levels normalizing between the second and fourth postoperative weeks. Patients with permanent hypocalcemia, failed to recover their normal parathyroid

Table 3. Univariate analysis of clinicopathologic characteristics in postoperative hypocalcemia

Characteristic	Normocalcemia	Hypocalcemia	P-value
Sex			NS
Male	106 (92.2)	9 (7.8)	
Female	676 (90.0)	75 (10.0)	
Age (yr)	46.20 ± 11.14	46.93 ± 10.00	NS
Presence of Graves' disease			NS
No	765 (90.5)	80 (9.5)	
Yes	17 (81.0)	4 (19.0)	
Operation			NS
Total thyroidectomy	716 (90.5)	75 (9.5)	
Total thyroidectomy + MRND	66 (88.0)	9 (12.0)	
Diagnosis			NS
Papillary thyroid cancer	773 (90.3)	83 (9.7)	
Follicular thyroid cancer	5 (83.3)	1 (16.7)	
Medullary thyroid cancer	2 (100.0)	0 (0.0)	
Anaplastic thyroid cancer	2 (100.0)	0 (0.0)	
Mass size (cm)	1.06 ± 0.78	1.23 ± 1.07	NS
Multifocality			NS
Single	518 (90.4)	55 (9.6)	
Multiple (≥ 2)	264 (90.1)	29 (9.9)	
Extrathyroid extension			NS
No	305 (92.4)	25 (7.6)	
Yes	477 (89.0)	59 (11.0)	
Thyroiditis			NS
No	603 (91.4)	57 (8.6)	
Yes	179 (86.9)	27 (13.1)	
No. of identified parathyroid glands	3.05 ± 0.84	2.85 ± 1.01	NS
No. of preserved parathyroid glands	1.75 ± 0.97	0.68 ± 0.78	<0.001
Removed central lymph node	10.71 ± 5.96	13.29 ± 7.84	0.004
No. of central lymph node metastasis	1.59 ± 2.51	1.87 ± 3.66	NS
T stage			NS
Less than T2	303 (92.4)	25 (7.6)	
More than T3	479 (89.0)	59 (11.0)	

Values are presented as number (%) or mean \pm SD.

NS, not significant; MRND, modified radical neck dissection.

function, even though parathyroid glands were autotransplanted in two cases and the discolored parathyroid glands were left *in situ* without autotransplantation in two cases. Significantly more hypocalcemia developed in patients who had more dissected lymph nodes, and who had less preserved parathyroid glands. Graves' disease, thyroiditis, multifocality of lesion, and extrathyroidal extension of the lesion were not correlated with the development of hypocalcemia (Table 3).

One hundred ninety-one patients had four intraoperatively identified parathyroid glands without any parathyroid autotransplantation being done. These patients were divided into three groups based on the number of preserved parathyroid glands (as described above) in or-

der to know if the number of preserved parathyroid glands had an effect on the incidence of postoperative hypocalcemia. Group I included 22 patients, group II had 77 and group III had 92. Five patients (22.7%) in group I and 5 patients (6.5%) in group II had transient hypocalcemia ($P < 0.001$) (Table 4). No transient hypocalcemia occurred in group III and none of them developed permanent hypocalcemia (Table 4). In group I, the total serum calcium, ionized calcium, and iPTH level fell to 8.41 ± 0.72 mg/dL, 0.97 ± 0.89 mM/L, and 19.52 ± 10.86 pg/mL on POD 1, then recovered rapidly to 9.14 ± 0.63 mg/dL, 1.13 ± 0.15 mM/L, and 27.87 ± 17.44 pg/mL, respectively. In group II, the total serum calcium, ionized calcium, and iPTH level was 8.30 ± 0.63 mg/dL, 1.00 ± 0.12 mM/L, and 16.17 ± 7.35

Table 4. Incidence of hypocalcemia according to the number of preserved parathyroid glands in patients with four intraoperatively identified parathyroid glands

Group	No. of preserved parathyroid glands	Total (n = 191)	No. of transient hypocalcemia (%)	No. of permanent hypocalcemia (%)
I	1	22	5 (22.7)	0 (0)
II	2	77	5 (6.5)	0 (0)
III	3	63	0 (0)	0 (0)
III	4	29	0 (0)	0 (0)

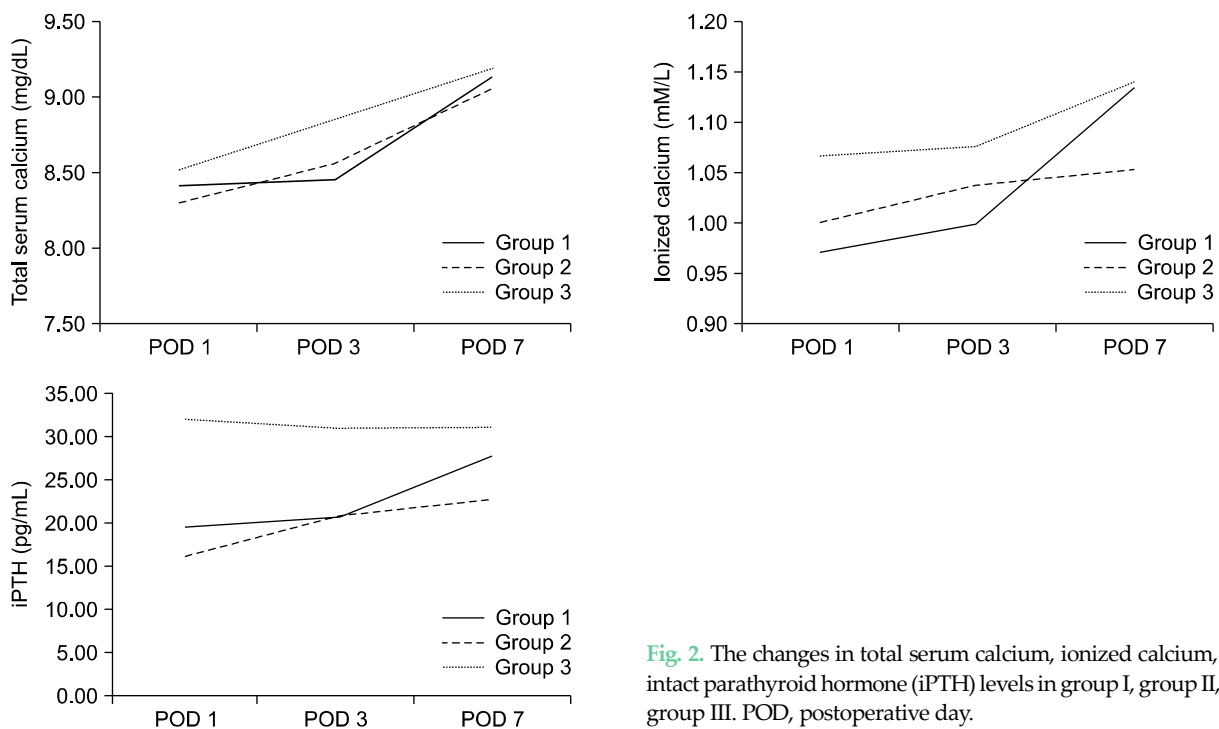


Fig. 2. The changes in total serum calcium, ionized calcium, and intact parathyroid hormone (iPTH) levels in group I, group II, and group III. POD, postoperative day.

pg/mL on POD 1, then rose to 9.06 ± 0.59 mg/dL, 1.05 ± 0.10 mM/L, and 22.70 ± 6.67 pg/mL, respectively. In group III, the total serum calcium, ionized calcium, and iPTH level was 8.52 ± 0.39 mg/dL, 1.07 ± 0.69 mM/L, and 32.08 ± 14.01 pg/mL on POD 1, then rose to 9.19 ± 0.37 mg/dL, 1.14 ± 0.15 mM/L, and 31.13 ± 9.85 pg/mL, respectively (Fig. 2). In group I, the results of the all blood tests were decreased to within the normal range on the first day after total thyroidectomy and were completely restored as similar values of group II and group III on the 7th day. There were no statistical differences in the parameters measured between group I, group II and group III on the 7th day. Two patients could not find one of the parathyroid gland and hypocalcemia occurred in both patients. Thirty three patients had one identified parathyroid glands and 5 patients (15.2%) had transient hypocalcemia and no permanent hypocalcemia. One hundred ninety-six patients had two parathyroid glands and 21 patients (10.7%) had transient hypocalcemia and 2 patients (1.0%) had permanent hypocalcemia. Three hundred forty one patients had three identified parathyroid glands and 26 patients (7.6%) had transient hypocalcemia and 2 patients (0.6%) had permanent hypocalcemia.

The removed central lymph nodes also related hypocalcemia significantly. Hypocalcemia was more common in twelve or more removed central lymph nodes (Table 5).

DISCUSSION

The incidence of thyroid surgery has increased in recent years due to the widespread use of ultrasonographic screening procedures. Thyroidectomy has been performed safely because of technical improvements and better knowledge of thyroid anatomy [11], however, postoperative

complications can still occur even with experienced surgeons. The well known complications that can occur after thyroid surgery are bleeding, parathyroid insufficiency, and injury to the recurrent laryngeal nerve [2,3,12-14]. Among them, parathyroid insufficiency is somewhat problematic in that the preservation of parathyroid glands particularly difficult during total thyroidectomy, because of the difficulty in identifying the normal parathyroid glands and in preserving their blood supply even with meticulous dissection.

The incidence of transient and permanent hypocalcemia in this paper was 9.2%, and 0.5%, respectively. The frequency is comparable to previous reports of patients who had thyroidectomy [5,7,11,15,16]. The patients with transient hypocalcemia were given oral calcium and vitamin D supplements to stabilize their calcium levels, thereafter, spontaneous normalization of their serum calcium levels gradually occurred within 1 month. The better known risk factors of postoperative hypocalcemia are parathyroid injury, parathyroid devascularization, extensive lymph node dissection, and Graves' disease [2-6,17,18]. It was known that patients with Graves' disease were associated with a higher incidence of postoperative hypocalcemia [4,7]. In the present study, 21 patients have been treated for Graves' disease at the time of operation. The incidence of hypocalcemia was 19.0% among patients with Graves' disease, which was higher than the incidence of hypocalcemia in patients without Graves' disease (9.5%). However, there was no correlation between the presence of Graves' disease and the development of hypocalcemia.

In the present study, the risk factors for developing postoperative hypocalcemia were extensive central node dissection and unsuccessful preservation of the parathyroid glands. Extensive central node dissection has been identified as a risk factor for hypocalcemia by Thompson et al. [1]. The dissection may increase the risk of injury to the inferior parathyroid glands and their blood supply. However, the parathyroid glands and their blood supply can be separated from the thyroid gland and the central node group within the fat by meticulous dissection. There is some sort of a boundary, by carefully dissecting the overlying fascia, between the parathyroid glands and their blood supply within the thymic tissue and the central

Table 5. Incidence of hypocalcemia according to the number of removed central lymph nodes (n = 866)

No. of removed central lymph nodes	Total	No. of transient hypocalcemia (%)	No. of permanent hypocalcemia (%)
0-11	540	41 (7.6)	1 (0.2)
12 or more	326	39 (12.0)	3 (0.9)

node group within the fat. An elevated level of care should be employed when a central node dissection is to be conducted.

There are many reasons why attempts at preserving the parathyroid glands may fail. Parathyroid glands may not be successfully preserved if they are located anterior to or within thyroid gland. Parathyroid glands that were removed intentionally and then implanted into muscle can also fail to survive. Direct trauma to the parathyroid gland that cause gland discoloration tend to result in the parathyroid gland not being preserved. The injury of blood supply of parathyroid glands unintentionally causes implantation or removal of the parathyroid glands. Thomusch et al. [4] emphasized that at least 2 parathyroid glands should be identified and preserved to prevent hypoparathyroidism and they found that no additional benefit was evident by having more than two identified and preserved parathyroid glands. In our study, the number of parathyroid gland identified during the operation was zero in 0.2% of cases, one in 3.8% cases, two in 22.6%, three in 39.4%, and four in 33.9%. The rate of preservation of more than one parathyroid gland was 69.7% in one identified parathyroid gland, 76.1% in two, 88.6% in three, and 94.9% in four. The higher the rate of parathyroid gland detection, the more chances of successfully preserving the parathyroid glands. The surgeon should make an attempt to identify as many of the parathyroid glands as possible.

Attie and Khafif [11] suggested that at least two functional parathyroid glands were necessary to avoid hypocalcemia, and Wingert et al. [7] suggested that resection of at least 2 parathyroid glands increased the risk of hypocalcemia. Kihara et al. [19] evaluated 83 patients wherein parathyroid preservation was attempted, and the number of successfully preserved parathyroid glands was 1.7, similar to what was achieved in our study. The incidence of permanent hypoparathyroidism in their study was 1.2%. No permanent hypocalcemia occurred among patients with at least one preserved parathyroid gland in our study. They reported that the serum calcium decreased to the low normal levels, and the serum iPTH levels were reduced to below the normal range in some of their patients with one or two preserved parathyroid glands on POD 1. In the group who had below normal iPTH levels, recovery to-

wards their preoperative values was almost complete at 30 days after the operation. But in the group whose iPTH levels fell below the detectable limit, the parathyroid function recovered to only 70% of their preoperative values [19]. In our study, in the group I and II patients with transient hypocalcemia, the serum calcium, ionized calcium, and iPTH levels were reduced within one day after operation, and return to the similar range within seven day as other studies [6,7,20], and there are no different levels between two groups. In some patients with one preserved parathyroid gland, the serum iPTH levels were reduced to below the normal range but not to below the detectable limit and they were able to completely recover to the normal range.

In conclusion, the number of preserved parathyroid glands is the most important factor for predicting permanent hypocalcemia and we found that only one functional parathyroid gland was needed to avoid permanent hypocalcemia. Even if all the parathyroid glands cannot be completely accounted for, the surgeon should make an attempt at identifying and preserving parathyroid glands without damaging their blood supply.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

REFERENCES

1. Thompson NW, Olsen WR, Hoffman GL. The continuing development of the technique of thyroidectomy. *Surgery* 1973;73:913-27.
2. Shaha AR, Jaffe BM. Parathyroid preservation during thyroid surgery. *Am J Otolaryngol* 1998;19:113-7.
3. Cheah WK, Arici C, Ituarte PH, Siperstein AE, Duh QY, Clark OH. Complications of neck dissection for thyroid cancer. *World J Surg* 2002;26:1013-6.
4. 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. *Surgery* 2003;133:180-5.
5. McHenry CR, Speroff T, Wentworth D, Murphy T. Risk factors for postthyroidectomy hypocalcemia. *Surgery* 1994;

- 116:641-7.
6. Demeester-Mirkine N, Hooghe L, Van Geertruyden J, De Maertelaer V. Hypocalcemia after thyroidectomy. *Arch Surg* 1992;127:854-8.
 7. Wingert DJ, Friesen SR, Iliopoulos JL, Pierce GE, Thomas JH, Hermreck AS. Post-thyroidectomy hypocalcemia. Incidence and risk factors. *Am J Surg* 1986;152:606-10.
 8. Shaha AR, Burnett C, Jaffe BM. Parathyroid autotransplantation during thyroid surgery. *J Surg Oncol* 1991;46:21-4.
 9. Olson JA Jr, DeBenedetti MK, Baumann DS, Wells SA Jr. Parathyroid autotransplantation during thyroidectomy. Results of long-term follow-up. *Ann Surg* 1996;223:472-8.
 10. Lee NJ, Blakey JD, Bhuta S, Calcaterra TC. Unintentional parathyroidectomy during thyroidectomy. *Laryngoscope* 1999;109:1238-40.
 11. Attie JN, Khafif RA. Preservation of parathyroid glands during total thyroidectomy. Improved technic utilizing microsurgery. *Am J Surg* 1975;130:399-404.
 12. Kark AE, Kissin MW, Auerbach R, Meikle M. Voice changes after thyroidectomy: role of the external laryngeal nerve. *Br Med J (Clin Res Ed)* 1984;289:1412-5.
 13. Crumley RL, Smith JD. Postoperative chylous fistula prevention and management. *Laryngoscope* 1976;86:804-13.
 14. Shaha AR, Jaffe BM. Practical management of post-thyroidectomy hematoma. *J Surg Oncol* 1994;57:235-8.
 15. Farrar WB, Cooperman M, James AG. Surgical management of papillary and follicular carcinoma of the thyroid. *Ann Surg* 1980;192:701-4.
 16. Attie JN, Moskowitz GW, Margouleff D, Levy LM. Feasibility of total thyroidectomy in the treatment of thyroid carcinoma: postoperative radioactive iodine evaluation of 140 cases. *Am J Surg* 1979;138:555-60.
 17. Lal G, Ituarte P, Kebebew E, Siperstein A, Duh QY, Clark OH. Should total thyroidectomy become the preferred procedure for surgical management of Graves' disease? *Thyroid* 2005;15:569-74.
 18. Pesce CE, Shiue Z, Tsai HL, Umbricht CB, Tufano RP, Dackiw AP, et al. Postoperative hypocalcemia after thyroidectomy for Graves' disease. *Thyroid* 2010;20:1279-83.
 19. Kihara M, Yokomise H, Miyauchi A, Matsusaka K. Recovery of parathyroid function after total thyroidectomy. *Surg Today* 2000;30:333-8.
 20. Percival RC, Hargreaves AW, Kanis JA. The mechanism of hypocalcaemia following thyroidectomy. *Acta Endocrinol (Copenh)* 1985;109:220-6.