

# Postoperative Hypoparathyroidism in Total Thyroidectomy: Incidence and Predictive Factors

## *Total Tiroidektomi Sonrası Gözlenen Hipoparatiroidizm İnsidensi ve Prediktif Faktörler*

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### Abstract

**Objective:** Total thyroidectomy is increasingly accepted as a choice of treatment not only for malignant but also for benign thyroid disorders. Nowadays, postoperative hypocalcaemia is the major concern in total thyroidectomy. The aim of this study is to quantify risk factors contributing to postoperative hypocalcaemia rates.

**Material and methods:** Medical records of 88 patients who underwent total thyroidectomy from 2000 to 2004 were reviewed. In addition to demographic information, postoperative hypocalcaemia and related risk factors were identified.

**Results:** The most common indication for total thyroidectomy was multinodular goiter (53.4%). One patient with anaplastic thyroid carcinoma died because of respiratory failure (1.1%). Temporary and permanent hypoparathyroidism rates were 26.1% and 3.4 %, respectively. Parathyroid reimplantation was performed to 7 patients (7.9%). Indication of surgery was statistically associated with an increased incidence of hypocalcaemia (P=0.019 for thyroid carcinoma and P=0.005 for completion thyroidectomy), whereas, sex, age, neck dissection and parathyroid reimplantation were not.

**Conclusions:** Postoperative hypocalcaemia is the major concern for thyroid surgeons. Completion and total thyroidectomy for thyroid malignancy increased postoperative hypoparathyroidism. With meticulous attention to operative technique and anatomical detail, surgeons can achieve low morbidity rates. *Turk Jem 2007; 11: 16-9*

**Key words:** Total thyroidectomy, hypocalcaemia, hypoparathyroidism

### Özet

**Amaç:** Total tiroidektomi, günümüzde, malign olduğu kadar, benign tiroid hastalıklarında da kullanılan cerrahi yöntemdir. Postoperatif hipokalsemi, total tiroidektomilerden sonra karşımıza çıkabilecek major bir komplikasyondur. Bu çalışmada, postoperatif hipokalsemiler için olası risk faktörlerini ortaya koymayı amaçladık.

**Gereç ve Yöntem:** 2000–2004 yılları arasında, değişik sebeplerden dolayı total tiroidektomiye maruz kalmış olan 88 hasta retrospektif olarak değerlendirildi. Postoperatif hipokalsemi oranları ve bunla ilgili risk faktörleri değerlendirildi.

**Bulgular:** Total tiroidektomi için en fazla endikasyonu multinodüler guatr oluşturdu (%53.4). Mortalite 1 hastada gözlemlendi (%1.1). Geçici ve kalıcı hipokalsemi oranları sırasıyla %26.1 ve %3.4 idi. Yedi hastaya paratiroid reimplantasyonu yapıldı. Cerrahi endikasyon ve postoperatif hipokalsemi oranları arasında anlamlı bir ilişki gözlemlendi (tiroid kanserleri için p=0.019 ve tamamlayıcı tiroidektomiler için p=0.005). Bununla birlikte, hastanın yaşı, cinsiyeti, boyun diseksiyonu ve paratiroid reimplantasyonu ile istatistiksel bir ilişki yoktu.

**Sonuç:** Tamamlayıcı tiroidektomiler ve tiroid kanserleri için gerçekleştirilen total tiroidektomiler, postoperatif hipokalsemi açısından risk faktörleridir. Anatomi bilgilerin ışığı altında dikkatli bir cerrahi teknik ile postoperatif hipokalsemi oranları oldukça azaltılabilecektir. *Turk Jem 2007; 11: 16-9*

**Anahtar kelimeler:** Total tiroidektomi, hipokalsemi, hipoparatiroidizm

### Introduction

Total thyroidectomy (TT) is performed for thyroid malignancy, toxic thyroid disease, multinodular goiter (MNG), thyroiditis and even parathyroid diseases such as malignancies (1-4). An increasing

proportion of thyroid operations are now done as total thyroidectomy (5). The only real argument against total thyroidectomy is the potential for an increased risk of complications. Total thyroidectomy carries potential risk to all parathyroid glands and both recurrent laryngeal nerves.

Transient hypocalcaemia and permanent hypoparathyroidism are well-known sequels of TT (6). Therefore, it is crucial to be aware of the incidences and to identify potential predictive clinical factors for these morbidities.

This study was undertaken to determine the postoperative incidence and predictive factors of the hypoparathyroidism in patients who underwent TT in a single center.

## Material and Methods

From November 2000 to November 2004 88 consecutive patients underwent total thyroidectomy. There were 79 women and 9 men with a mean age of 46.65 years (range 17 to 74). All patients had routine biochemical determinations, thyroid function tests and chest radiographs. The preoperative work-up consisted of thyroid ultrasound, fine needle aspiration cytology (FNAC), motility control of vocal cords through indirect laryngoscopy. Thyroid scintigraphy was performed selectively. Indications for surgery included multinodular goiter (MNG) (n=38), toxic MNG (n=9), toxic diffuse goiter (n=11), non-toxic diffuse goiter (diagnosed as Hashimoto thyroiditis in pathological examination, n=5), thyroid carcinoma (n=17) (Table 1). Completion thyroidectomy for recurrent goiter was performed in 8 patients. After the permanent histopathological specimens demonstrated carcinoma at initial thyroidectomy, completion thyroidectomy was performed in 4 patients. A modified neck dissection was performed in 5 patients with clinically evident or biopsy proved bulky lymphadenopathy. Two patients had deliberate partial resection of a recurrent laryngeal nerve involved with thyroid carcinoma. Surgery was performed by staff general surgeons in our center or by trainees under their supervision following classical operation procedures. Total dissection of the recurrent nerve over its entire cervical course until they entered the larynx was performed. Careful dissection was also performed along the thyroid capsule attempting to identify and preserve parathyroid glands with their vascular supply. If it was necessary to devascularize or separate the parathyroid gland from its surrounding structures or if a parathyroid gland was identified within the resected specimen, it was auto transplanted into the sternocleidomastoid muscle (n=7).

All patients underwent indirect laryngoscopic examination of vocal cords by an otolaryngologist and total serum calcium and phosphorus levels were measured twice in the first 24 h postoperatively. Serum PTH level was also measured when serum calcium level < 8 mg/dl with or without symptoms such as tetany, muscle spasm and peroral paresthesia was obtained. Patients were considered to have permanent hypopa-

**Table 1. Indications of total thyroidectomy (n=88)**

Indication	n	%
MNG	38	43
Toxic MNG	9	10
Toxic diffuse goiter	11	12.5
Diffuse non-toxic goiter	5	5.7
Thyroid carcinoma	17	19.3
Recurrent goiter	8	9
Total	88	100

rathyroidism if they still required daily doses of 1,25-dihydroxycholecalciferol or calcium lactate and their PTH levels were below the normal range after 12 months postoperatively. Follow ups were recorded in a computerized database.

Data were analyzed by Chi Square test or unpaired t-test, and differences were regarded as significant when the P value was less than 0.05.

## Results

The mortality rate was 1.1% (n=1). The elderly woman with anaplastic thyroid carcinoma died because of respiratory failure. There were 4 hematomas (3 superficial and 1 deep), 1 abscess and 1 hemorrhage which required re-exploration with no further complications.

Overall, 26 patients (29.5%) were identified with postoperative hypocalcaemia. The rates of transient and permanent hypoparathyroidism were 26.1% and 3.4%, respectively. Parathyroid reimplantation was performed to 7 patients. Two of these 7 autotransplanted patients had postoperative hypocalcaemia (28.6%).

The rates of temporary and permanent hypoparathyroidism were higher after total thyroidectomy for malignancy and completion thyroidectomy (p<0.05, t test). However, no statistically significant associations between the occurrence of hypocalcaemia, sex, age parathyroid reimplantation or thyrotoxicosis were identified (Table 2).

Temporary and permanent recurrent inferior laryngeal nerve palsy rates were 5.7% and 0% respectively.

## Discussion

Postoperative hypocalcaemia after total thyroidectomy has been reported to range from 0% to 68% (5,7-13). This phenomenon may be transient or permanent. Transient biochemical hypocalcaemia has been reported in the majority of the patients following thyroid surgery, not as a complication but as a treatment problem (5). The risk of permanent hypoparathyroidism following thyroidectomy varies from 0 up to 10% (4,13-18). This dire complication is a major concern for thyroid surgeons and subjects patients to lifelong requirement of calcium and vitamin

**Table 2. Incidence of hypocalcemia for different risk factors**

Variable	hypocalcemia (%)	p
Sex		
Male	22.2	NS
Female	30.4	
Indication of surgery		
Thyroid carcinoma	52.9	0.019
MNG	21.8	NS
Graves	27.3	NS
Completion thyroidectomy	66.7	0.005
Neck dissection		
Yes	60	NS
No	27.7	
Parathyroid reimplantation		
Yes	28.6	NS
No	29.6	

D supplement. In the present study the rates of transient and permanent hypoparathyroidism were 26.1% and 3.4% respectively. These rates compare favorably with other series those are performed by endocrine surgeons mostly (Table 3).

Controversy still exists regarding factors that are associated with postoperative hypocalcaemia. Multiple factors may play role in pathogenesis of postoperative hypoparathyroidism such as hemodilution (6), hungry bone syndrome, medications and general anesthesia (13). Recently, Bhattacharyya and coworkers reported that younger age was statistically associated with an increased incidence of hypocalcaemia (2), whereas other series revealed that older patient age carry an increased risk (19). It's conceivable that the ability of parathyroid glands to recover from operative trauma may decrease with older age. However, in the current series, age does not play significant role in postoperative hypocalcaemia. Prevalent of vitamin D deficiency and poor calcium intake and skeletal calcium reserves may play role in the transient hypocalcaemia (20). In patients experiencing significant hypocalcaemia and permanent hypoparathyroidism, the most probable causes are trauma, devascularization or inadvertent excision of one or more parathyroid glands during surgery. Bergamaschi and coworkers found that thyroidectomy with node dissection and completion thyroidectomy are risk factors for permanent hypoparathyroidism (1). In the other studies, it has been showed that permanent hypoparathyroidism is slightly more frequent in cases of thyroidectomy for hypothyroidism, thyroid carcinoma or completion thyroidectomy (21,22). This could be explained by technical difficulties of parathyroid preservation or impairment of parathyroid blood flow during dissection in this condition. The findings that hypocalcaemia is mostly associated with completion thyroidectomy and malignancy in our study, corresponds with the published series (21-24). There were 3 patients who had permanent hypoparathyroidism and this rate failed to reach statistical significance owing to the small sample size to reveal risk factors for permanent hypoparathyroidism (1 patient had MNG with large thyroid volume and 2 patients had thyroid malignancy).

The preservation of parathyroid tissue is mandatory to obviate the terrible consequences of permanent hypoparathyroidism. Parathyroid glands should retain in situ with an intact blood

supply (15). Parathyroid autotransplantation should be considered when parathyroid glands are resected or devascularised (14). It has been shown that incidence of permanent hypoparathyroidism after autotransplantation during TT is reduced to nearly zero (3,25). Based on this fact, some authors advocated the routine autotransplantation of at least one parathyroid gland in every case of TT especially with large volume (5). Conversely, others question the safety of parathyroid autotransplantation. Also, this procedure could induce postoperative transient hypocalcaemia (21). We performed parathyroid autotransplantation in 7 cases and 2 of them had postoperative transient hypocalcaemia (28.6%). This is not significant as to deduce that parathyroid autotransplantation induces postoperative hypocalcaemia. Besides, the lack of thyroid gland volume measurement is the limitation of this study. However the measurement of thyroid volume was not being performed routinely in our clinic up till now; so we could not achieve the data about the gland sizes preoperatively.

It's also prudent to examine thyroidectomy specimen carefully, when risk factors for inadvertent parathyroidectomy are present, with the intent of identifying normal parathyroid glands that may be suitable for autotransplantation (26). We disclosed two parathyroid glands during examination of thyroidectomy specimen in two cases and autotransplanted them after confirming histopathologically. It has been advised that histopathologic confirmation of glands before autotransplantation was performed (26).

Most important factor to perform total thyroidectomy safely is appropriate training. Many authors believe that general surgery training programs don't give adequate exposure to thyroid surgery (9,27). Lamade and coworkers reported nearly two times fold incidence of recurrent laryngeal nerve (RLN) palsy for surgeons who had completed only general surgery training program but were not specializing in thyroid surgery, compared with surgical trainees and surgeons who specialized in thyroid surgery (28). Other factors that are important in performing safe and an affective thyroid surgery include hospital operative volume and the experience of surgeon (12,29). Sosa and coworkers reported that the individual surgeon's experience rather than the hospital's experience, significantly correlated with

**Table 3. Postoperative hypoparathyroidism after total thyroidectomy**

Study	Year	No of patients	Hypocalcaemia (%)	
			Permanent	transient
Dener (7)	2002	102	0	0.9
Rosato (18)	2002	14934	2.2	14
Bron (4)	2004	834	2.4	14.4
Bhattacharyya (2)	2002	517	?	6.2
Liu (16)	1998	106	0	3.7
Wilson (13)	2000	50	0	68
Kihara (15)	2000	92	4.3	?
Pappolardo (10)	1998	69	3	35
De Toma (14)	1995	79	7.5	13.5
Hisham (8)	2001	98	0	27
Current series	2006	88	3.4	26.1

complication rates (12). In the present study major complication rates are comparable to those in previously published large series about total thyroidectomy (TT). We believe that general surgeons who have been well trained in the techniques of thyroid surgery can perform TT within minimal morbidity rates. However, this experience can be given by surgery training program in the hospitals with at least moderately high operative volume (50-150 operation per year) (30), as in our center.

As a conclusion, one of the major complications of TT is permanent hypoparathyroidism. On the other hand, postoperative transient hypocalcaemia is a major surgical concern. The incidence of this problem is higher after total thyroidectomy for malignancy and completion the thyroidectomy.

## References

- Bergamaschi R, Becouarn G, Ronceray J, Arnaud JP. Morbidity of thyroid surgery. *Am J Surg* 1998; 176: 71-5.
- Bhattacharyya N, Fried M. Assessment of the morbidity and complications of total thyroidectomy. *Arch Otolaryngol Head Neck Surg* 2002; 128: 389-92.
- Bliss RD, Gauger PG, Delbridge LW. Surgeon's approach to the thyroid gland: surgical anatomy and the importance of technique. *World J Surg* 2000; 24: 891-7.
- Bron LP, O'Brien CJ. Total thyroidectomy for clinically benign disease of the thyroid gland. *Br J Surg* 2004; 91: 569-74.
- Delbridge L, Guinea AI, Reeve TS. Total thyroidectomy for bilateral benign multinodular goiter: effect of changing practice. *Arch Surg* 1999; 134: 1389-93.
- Demeester-Mirkine N, Hooghe L, Van Geertruyden J, De Maertelaer V. Hypocalcemia after thyroidectomy. *Arch Surg* 1992; 127: 854-8.
- Dener C. Complication rates after operations for benign thyroid disease. *Acta Otolaryngol* 2002; 122: 679-83.
- Hisham AN, Azlina AF, Aina EN, Sarajah A. Total thyroidectomy: the procedure of choice for multinodular goitre. *Eur J Surg* 2001; 167: 403-5.
- Mc Henry CR. Patient volumes and complications in thyroid surgery. *Br J Surg* 2002; 89: 821-3.
- Pappalardo G, Guadalaxara A, Frattaroli FM, Illomei G, Falaschi P. Total compared with subtotal thyroidectomy in benign nodular disease: personal series and review of published reports. *Eur J Surg* 1998; 164: 501-6.
- Reeve TS, Curtin A, Fingleton L, Kennedy P, Mackie W, Porter T, Simons D, Townend D, Delbridge L. Can total thyroidectomy be performed as safely by general surgeons in provincial centers as by surgeons in specialized endocrine surgical units? Making the case for surgical training. *Arch Surg* 1994; 129: 834-6.
- Sosa JA, Bowman HM, Tielsch JM, Powe NR, Gordon TA, Udelsman R. The importance of surgeon experience for clinical and economic outcomes from thyroidectomy. *Ann Surg* 1998; 228: 320-30.
- Wilson RB, Erskine C, Crowe PJ. Hypomagnesemia and hypocalcaemia after thyroidectomy: prospective study. *World J Surg* 2000; 24: 722-6.
- De Toma G, Tedesco M, Gabriele R, Campi M, Plocco M, Borghese M, Letizia C. Total thyroidectomy in the treatment of multinodular toxic goiter. *G Chir* 1995; 16: 373-6.
- Kihara M, Yokomise H, Miyauchi A, Matsusaka K. Recovery of parathyroid function after total thyroidectomy. *Surg Today* 2000; 30: 333-8.
- Liu Q, Djuricin G, Prinz RA. Total thyroidectomy for benign thyroid disease. *Surgery* 1998; 123: 2-7.
- Olson JA Jr, DeBenedetti MK, Baumann DS, Wells SA Jr. Parathyroid autotransplantation during thyroidectomy. Results of long-term follow-up. *Ann Surg* 1996; 223: 472-80.
- Rosato L, Avenia N, Bernante P, De Palma M, Gulino G, Nasi PG, Pelizzo MR, Pezzullo L. Complications of thyroid surgery: analysis of a multicentric study on 14,934 patients operated on in Italy over 5 years. *World J Surg*. 2004; 28: 271-6.
- Miccoli P, Vitti P, Rago T, Iacconi P, Bartalena L, Bogazzi F, Fiore E, Valeriano R, Chiovato L, Rocchi R, Pinchera A. Surgical treatment of Graves' disease: subtotal or total thyroidectomy? *Surgery* 1996; 120: 1020-5.
- Mishra A, Agarwal G, Agarwal A, Mishra SK. Safety and efficacy of total thyroidectomy in hands of endocrine surgery trainees. *Am J Surg* 1999; 178: 377-80.
- Pattou F, Combemale F, Fabre S, Carnaille B, Decoux M, Wemeau JL, Racadot A, Proye C. Hypocalcaemia following thyroid surgery: incidence and prediction of outcome. *World J Surg* 1998; 22: 718-24.
- Sasson AR, Pingpank JF Jr, Wetherington RW, Hanlon AL, Ridge JA. Incidental parathyroidectomy during thyroid surgery does not cause transient symptomatic hypocalcaemia. *Arch Otolaryngol Head Neck Surg* 2001; 127: 304-8.
- See AC, Soo KC. Hypocalcaemia following thyroidectomy for thyrotoxicosis. *Br J Surg* 1997; 84: 95-7.
- Yamashita H, Noguchi S, Tahara K, Watanabe S, Uchino S, Kawamoto H, Toda M, Murakami N. Postoperative tetany in patients with Graves' disease: a risk factor analysis. *Clin Endocrinol (Oxf)* 1997; 47: 71-7.
- Zedenius J, Wadstrom C, Delbridge L. Routine autotransplantation of at least one parathyroid gland during total thyroidectomy may reduce permanent hypoparathyroidism to zero. *Aust N Z J Surg* 1999; 69: 794-7.
- Lin DT, Patel SG, Shaha AR, Singh B, Shah JP. Incidence of inadvertent parathyroid removal during thyroidectomy. *Laryngoscope* 2002; 112: 608-11.
- Harness JK, Organ CH Jr, Thompson NW. Operative experience of U.S. general surgery residents in thyroid and parathyroid disease. *Surgery* 1995; 118: 1063-70.
- Lamade W, Renz K, Willeke F, Klar E, Herfarth C. Effect of training on the incidence of nerve damage in thyroid surgery. *Br J Surg* 1999; 86: 388-91.
- Kotan C, Kosem M, Algun E, Ayakta H, Sonmez R, Soylemez O. Influence of the refinement of surgical technique and surgeon's experience on the rate of complications after total thyroidectomy for benign thyroid disease. *Acta Chir Belg* 2003; 103: 278-81.
- Thomusch O, Machens A, Sekulla C, et al. Multivariate analysis of risk factors for postoperative complications in benign goiter surgery: prospective multicenter study in Germany. *World J Surg* 2000; 24: 1335-41.