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ORIGINAL ARTICLE

Determination of risk factors causing hypocalcaemia after thyroid surgery

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Summary *Objective:* The most common complication after thyroid surgery is hypocalcaemia and it sometimes leads to problems that are difficult to correct in patients. The present study was aimed to determine the risk factors causing the development of hypocalcaemia after thyroid surgery.

Methods: 818 adult patients were included in the study. The data were recorded by examining the hospital automation system and patient files retrospectively. Patients' demographic characteristics, radiological imaging findings, serum biochemical parameters, extent of the performed surgery, histopathological diagnoses were recorded.

Results: The rate of hypocalcaemia was 28.4% (1.7% permanent). In multivariate analysis: the female gender ($p = 0.002$), heavier thyroid gland ($p = 0.084$), substernal location ($p = 0.004$) and cervical lymph nodes dissection (CLND) ($p < 0.001$) were found to be significantly. Malignant thyroid pathology ($p = 0.006$) and total thyroidectomy ($p = 0.025$) increased the risk of hypocalcaemia significantly in univariate analysis. However, this increase in risk was not found to be statistically significant in regression analysis. Significant statistical result was not found on postoperative hypocalcaemia in terms of advanced age, hyperthyroidism and re-operation. The duration of hospitalization was higher in patients with postoperative hypocalcaemia ($m = 2$ days) ($p < 0.001$).

Conclusion: In our analyses CLND, female gender, substernal location and heavier thyroid gland was found to be the independent risk factors in the development of postoperative hypocalcaemia. The development of postoperative hypocalcaemia may be predicted and measures may be taken to prevent clinical findings.

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1. Introduction

Hypocalcaemia is the most common complication after thyroid surgeries and may have long-term consequences for both the patient and the surgeons.[1–3] The developing hypocalcaemia after thyroidectomy may often be due to disruption of parathyroid glands blood supply, inadvertent parathyroidectomy, venous drainage disorder, dilutional hypocalcaemia, hungry bone syndrome.[4] In the current publications, the rate of transient hypocalcaemia was 19–38% and the rate of permanent hypocalcaemia after surgery was 0–3% after surgery.[3] The factors that may cause the development of hypocalcaemia by utilizing literature data were determined as female gender, advanced age, hyperthyroidism, malignant thyroid pathology, re-operation, substernal localization of thyroid tissue, cervical lymph node dissection (CLND) and the heavier thyroid gland.

The aim of present study was to detect the causes of postoperative hypocalcaemia and to prevent the clinical symptoms related to hypocalcaemia by determining the measures for these reasons before surgery.

2. Material and method

2.1. Patients

Patients who underwent surgery due to benign or malignant diseases of the thyroid gland in the General Surgery Clinic of Erciyes University Medical Faculty Hospital between January 2010 and June 2016 were included in our study. After the patients with diseases, other than thyroid gland, as primary/secondary/tertiary hyperparathyroidism, paraneoplastic hypercalcemia or any other malignant disease with bone involvement were excluded, a total of 818 adult patients were evaluated in our study. All data of the patients were obtained retrospectively by examining hospital automation system and clinical patient files. The patients' demographic characteristics, radiological imaging methods, serum biochemical values, histopathological diagnoses, specimen weights, extent of surgery, performing CLND were recorded. Retrosternal goitre was defined by ultrasonography or computerized tomography evaluation as one that either descends below the thoracic inlet, or has more than 50% of its volume below this level. Pathological diagnoses of thyroid disease were categorized as single diagnosis whether a pathological diagnosis is accompanied by another accompanying disease or not. A two-disease entity at the same time was not assigned as discrete subgroup. In all patients, serum calcium levels measured at 24 h, 72 h, 1, 3, 6, 12 and 18 months after surgery were recorded.

2.2. Hypocalcaemia

The findings, which are occurred due to the fact that the calcium level is lower than 8 mg/dl at 24 and 72 h after thyroidectomy, such as the numbness in the perioral area and in the distal of extremities, and the positive Chvostek and Trousseau signs, and the prolongation of QT-interval in the electrocardiogram, are defined as the hypocalcaemia. Patients of hypocalcaemia treated with medical therapy until postoperative first year were considered as temporary. Patients in need of exogenous calcium and vitamin D for more than one year were accepted as permanent hypocalcaemia.

2.3. Statistical analysis

The statistical analysis of the findings obtained from the study was performed with IBM SPSS 22.0 (SPSS Inc., Chicago, IL, USA) package program. The normal distribution of the data was evaluated by histogram, Q–Q plots and Shapiro–Wilk test. Nonparametric tests were used in evaluation of the quantitative data because parametric assumptions could not be obtained. Quantitative data were presented as median (1st quarter - 3rd quarter). The Mann–Whitney-U test was used for quantitative variables in comparisons between the binary groups. The Kruskal–Wallis test was used for comparisons of more than two groups. Dunn–Bonferroni test was used for multiple comparisons. Test statistics of categorical data were evaluated with Pearson's chi-squared and tested by Exact method. Logistic regression analysis was used for multivariate analysis. Significance level was accepted as $p < 0.05$ in univariate analyses. $p < 0.1$ was considered as statistically significant for multivariate analysis.

3. Results

The female/male ratio was found to be 3.52/1. The mean age of the patients was 46.2 (18–87) ($m = 46$) years. Transient hypocalcaemia developed in 218 (26.7%) patients and the permanent hypocalcaemia developed in 14 (1.7%) (Table 1). The patients' demographic characteristics, pathology reports, thyroid function test (TFT) results, specimen weights and extent of the performed surgery are shown in Table 1.

The cross-comparative results of the parameters that may cause postoperative hypocalcaemia are shown in Table 2. There were statistically significant results including parameters of the gender, the performing CLND, field of the CLND, the substernal localization of thyroid tissue, the pathology results and extent of the performed surgery. However, there was no statistically significant finding between the postoperative hypocalcaemia and the age of

Table 1 Demographic and other characteristics of patients.

Demographic and other characteristics	n = 818(%)
Age	46,3 (18–87)
Gender	
Female	637 (77,9)
Male	181 (22,1)
Specimen Weight	72,8 g (6–500 g)
Thyroid Function Test	
Euthyroid	576 (70,4)
Hypothyroid	39 (4,8)
Hyperthyroid	203 (24,8)
Thyroid Pathology	
Benign	633 (77,4)
Nodular Colloidal Goitre	416 (65,7)
Graves' Disease	80 (12,6)
Toxic Nodular Goitre	78 (12,4)
Hashimoto's Thyroiditis	54 (8,5)
De Quervain's Thyroiditis	3 (0,5)
Riedel Thyroiditis	2 (0,4)
Malign	185 (22,6)
Papillary CA	167 (90,3)
Follicular CA	13 (7,0)
Medullary CA	1 (0,5)
Anaplastic CA	2 (1,1)
Squamous cell CA	2 (1,1)
Substernal Localization	
Yes	84 (10,3)
No	734 (89,7)
Lymph Node Dissection	53 (6,5)
CND	34 (64,2)
CUND	15 (28,3)
CBND	4 (7,5)
Re-operation	
Yes	49 (6,0)
No	769 (94,0)
Types of Thyroid Surgery Performed	
Hemithyroidectomy	63 (7,7)
Total thyroidectomy	755 (92,3)
Postoperative Hypocalcaemia	
Transient	218 (26,7)
Permanent	14 (1,7)

CND: Central Neck Dissection.
CUND: Central + Unilateral Neck Dissection.
CBND: Central + Bilateral Neck Dissection.

patients, TFT results, re-operation situation, benign and malignant thyroid pathologies subtypes (Table 2).

Female gender was 2.78-fold increased risk of development of hypocalcaemia compared to male gender. This increase was found to be significant in multivariate analyses ($p = 0.002$) (Table 3).

When the pathology reports of 818 patients were evaluated, it was seen that the weight of thyroid specimen was measured in only 381 of them. The mean thyroid specimen weight of these patients was 72.28 g, and the median value was 50 g (28 g in the first quarter, 90 g in the third quarter). Thyroid gland weights were found to be higher in patients with hypocalcaemia in multivariate analysis. ($p = 0.084$) (Table 3).

The substernal localization of the thyroid tissue increased the risk of developing postoperative hypocalcaemia by 2.73 times, which was significant in multivariate analyses ($p = 0.004$) (Table 3).

The risk of hypocalcaemia was observed 8.77 times higher in patients who underwent CLND ($p < 0.001$) in multivariate analyses (Table 3). When CLND extent was grouped, statistically significant differences were found in postoperative hypocalcaemia. However, because the number of patients was small, regression analysis could not be performed.

The risk of hypocalcaemia was 1.63 times higher in patients with malign thyroid pathology and 2.21 times higher in patients who underwent bilateral total thyroidectomy in univariate analyses significantly. However, they were not significant in regression analyses (Table 3).

The median value of the length of stay in hospital was 1 day. The shortest length of stay in hospital was 1 day and the longest length of stay in hospital was 9 days. The median length of stay was 1 day in patients without postoperative hypocalcaemia and 2 days in patients with postoperative hypocalcaemia. Longer hospital stay of the patients with postoperative hypocalcaemia was found to be significant ($p < 0.001$) (Table 4).

4. Discussion

Our results indicate that female gender, heavier thyroid gland, substernal localization and CLND were found to be independent risk factors causing postoperative hypocalcaemia. It was shown that the malignant thyroid pathology and the surgery performed in the form of total thyroidectomy increased the risk of hypocalcaemia significantly. However, this increase in risk was not found to be statistically significant in regression analyses. Significant statistical result was not found on postoperative hypocalcaemia in terms of advanced age, hyperthyroidism and reoperation.

Nowadays, there are many studies investigating the risk factors causing the development of hypocalcaemia after thyroidectomy. Although possible risk factors were evaluated in these studies, this subject still not been fully clarified.

In the literature, it was shown that the women are more prone to development of the postoperative hypocalcaemia because of pre and post-menopausal hormonal factors compared to the men. In this subject, the effects of hormonal variations on D-vitamin, parathyroid hormone (PTH) and calcium absorption are emphasised.[5] There are many studies showing that postoperative hypocalcaemia develops more frequently in women.[6–8] In a study conducted by Docimo G et al,[9] they found that the female gender was significant in univariate analyses, but in multivariate analyses it was not significant. In a comprehensive review by Eismontas V et al,[10] the female gender is an independent risk factor for the development of hypocalcaemia. It should be kept in mind that the more risk of female gender in our study may be based on the heterogeneous distribution of patients between the groups and the high number of female patients.

In studies conducted by Kamer E. et al,[11] Lindblom P. et al[12] and Weiss A. et al,[13] the elderly patients were more

Table 2 Cross analysis of multiple variables for postoperative hypocalcaemia development.

Variables		Hypocalcaemia		*P*
		No	Yes	
Age (mean)		46,4	45,98	0,588
Specimen Weight (mean)		68,4gr	84,6gr	**0,036**
Gender	Male	153 (84,5%)	28 (15,5%)	<**0,001**
	Female	433 (68,0%)	204 (32,0%)	
TFT	Euthyroid	416 (72,2%)	160 (27,8%)	0.826
	Hypothyroid	28 (70,0%)	11 (30,0%)	
	Hyperthyroid	142 (73,6%)	61 (26,4%)	
Re-operation	Yes	33 (67,3%)	16 (32,7%)	0,292
	No	553 (71,9%)	216 (28,1%)	
Cervical Lymph Node Dissection	Yes	22 (41,5%)	31 (58,5%)	<**0,001**
	No	564 (73,7%)	201 (26,3%)	
	CND	21 (61,8%)	13 (38,2%)	<**0,001**
	CUND	1 (6,3%)	14 (93,7%)	
	CBND	0 (−)	4 (100%)	
Substernal Localization	Yes	48 (57,1%)	36 (42,9%)	**0,002**
	No	538 (73,3%)	196 (26,7%)	
Pathology	Benign	467 (74,0%)	164 (26,0%)	**0,006**
	Malign	119 (63,6%)	68 (32,4%)	
Types of Thyroid Surgery	HT	53 (84,1%)	10 (15,9%)	**0,022**
	TT	533 (70,6%)	222 (29,4%)	
Benign Thyroid Pathology	NCG	318 (76,4%)	98 (23,6%)	0,082
	Graves' Disease	53 (66,3%)	27 (33,7%)	
	TNG	58 (74,4%)	20 (25,6%)	
	Hashimoto	37 (68,5%)	17 (31,5%)	
	De Quervain	1 (33,3%)	2 (66,7%)	
	Riedel Thyroiditis	1 (50,0%)	1 (50,0%)	
	Other benign patholog.	429 (74,7%)	145 (25,3%)	0,150
	Thyroiditis group	39 (66,1%)	20 (33,9%)	
Malign Thyroid Pathology	Papillary CA	109 (65,3%)	58 (34,7%)	0,180
	Follicular CA	8 (61,5%)	5 (38,5%)	
	Medullary CA	–	1 (100%)	
	Anaplastic CA	1 (50,0%)	1 (50,0%)	
	Other	–	2 (100%)	

The significance level was accepted as $p < 0.05$ in univariate analyses. $p < 0.1$ was considered as statistically significant for multivariate analysis.
TFT: Thyroid Function Tests, CND: Central Neck Dissection, CUND: Central + Unilateral Neck Dissection, CBND: Central + Bilateral Neck Dissection, HT: Hemithyroidectomy, TT: Total thyroidectomy, NCG: Nodular Colloidal Goitre, TNG: Toxic Nodular Goitre, CA: Cancer.

risky in the development of hypocalcaemia. In contrast to these studies, in studies conducted by Duclos A. et al,[6] Cho JN et al[7] and Hallgrimsson P et al,[14] the development of hypocalcaemia after thyroidectomy was observed more common in young patients. In the study conducted by Bähler S. et al,[15] similar to our study, there was no effect of age factor on the development of hypocalcaemia.

Hyperthyroidism accelerates the bone turnover and hungry bone syndrome develops in patients after thyroidectomy. Also, the postoperative hypocalcaemia may be developed due to difficulties in surgical dissection caused by increased vascularity in the patients with hyperthyroidism.[14] In this context, there are also many studies showing that hyperthyroidism is a risk factor for development of postoperative hypocalcaemia.[3,10,16,17] In few studies, the difference in TFT was not a factor in the development of hypocalcaemia in line with our study.[7]

Duclos A et al[6] and McHenry CR et al[18] revealed the development of hypocalcaemia increased in patients with thyroid tissue weight greater than 100 g. However, Karabeyoglu M et al[19] reported that patients with thyroid gland with less than 50 ml volume were significant in this sense. In our study, it should be taken into consideration that the statistically significant risk of the patients whose thyroid gland was heavier may be related to difference in the number of patients between the groups or missing data.

In malign thyroid pathologies, the hypocalcaemia may develop due to the vascular damage or the inadvertent parathyroidectomy due to invasion of thyroid capsule. Several studies reported that malignant histology increased the development of hypocalcaemia in line with the results of our study.[6,7,17,20] However, this increase was found to be insignificant in regression analyses, which was attributed to the imbalance in the number of patients in groups.

The surgical capsule of the thyroid gland shows adhesions to surrounding tissues due to inflammation in the presence of thyroiditis. Therefore, parathyroid glands may be damaged during dissection and hypocalcaemia may

Table 3 Univariate and multivariate analyses of multiple risk factors in terms of the postoperative hypocalcaemia development.

Risk Factors		Univariate Analysis		Multivariate Analysis	
		OR (Cl)	*p*	OR (Cl)	*p*
Gender	Male	1,00	–	1,00	–
	Female	2,57 (1,83–10,92)	<**0,001**	2,78 (1,47–5,27)	**0,002**
Age	Hypocalcaemia –	1,00	–		
	Hypocalcaemia +	0,998	0708		
Thyroid Function Tests	Euthyroid	1,00	–		
	Hypothyroid	1,02 (0,50–2,10)	0,954		
	Hyperthyroid	1,18 (0,79–1,59)	0,826		
Specimen Weight	Hypocalcaemia –	1,00	–	1,00	–
	Hypocalcaemia +	1.003 (1,000–1,005)	**0,036**	1,003 (1,000–1,006)	**0,084**
Pathology	Benign	1,00	–		
	Malign	1,63 (1,15–2,30)	**0,006**		
Types of Thyroid Surgery	HT	1,00	–		
	TT	2,21 (1,10–4,42)	**0,025**		
Substernal Localization	No	1,00	–	1,00	–
	Yes	2,06 (1,30–3,27)	**0,002**	2,73 (1,39–5,39)	**0,004**
Cervical Lymph Node Dissection	No	1,00	–	1,00	–
	Yes	3,95 (2,24–6,99)	<**0,001**	8,77 (3,05–25,17)	<**0,001**
Re-operation	No	1,00	–		
	Yes	1,24 (0,67–2,30)	0,493		

The significance level was accepted as $p < 0.05$ in univariate analyses. $p<0.1$ was considered as statistically significant for multivariate analysis.
OR: Odds Ratio, HT: Hemithyroidectomy, TT: Total thyroidectomy.

develop.[19] In the literature, it was mentioned that the frequency of hypocalcaemia increased after autoimmune thyroiditis.[17,21] In our study, when the patients with thyroiditis and the patients with other benign thyroid pathologies were compared, there was no statistically significant difference in the development of hypocalcaemia. Similarly, Ozemir IA et al[22] reported that the histology of thyroiditis was found to be insignificant in the development of hypocalcaemia.

There are studies showing that the postoperative hypoparathyroidism findings are more common in total thyroidectomy than hemithyroidectomy.[17,22–25] If we want to explain the development of this hypocalcaemia with a simple logic, we can say that the number of vascular structures with the possibility of injury and the number of inadvertent removals of parathyroid glands increases as the surgery area is extended. In our study, the total thyroidectomy increases the risk of hypocalcaemia when compared to hemithyroidectomy, which was not an independent risk factor in regression analyses. It can be attributed to the heterogeneity of the groups and the difference in the numbers of patient.

Table 4 Lengths of stay in hospital of the patients with and without postoperative hypocalcaemia.

	Hypocalcaemia		*p*
	No	Yes	
Length of stay in hospital (day)	1,0 (1,0–2,0)	2,0 (1,0–3,0)	<**0,001**

The significance level was accepted as $p < 0.05$ in univariate analyses. $p<0.1$ was considered as statistically significant for multivariate analysis.

Because the surgery is more complicated in retrosternal goitre, parathyroid gland blood supply may be impaired due to vascular injuries. In addition, we think that the development of hypocalcaemia after surgery is more common due to inadvertent parathyroidectomy as a result of atypical placement of the parathyroid glands because of the large thyroid tissue. In the literature, there are many studies that have findings in parallel to our study.[26] The risk of hypocalcaemia development was found 1.49 times in the study of Moten AS et al[27] and 1.77 times in the study of Bove A et al.[28]

The development of hypocalcaemia increases because of the damage of the vascular bed providing the blood supply of the parathyroid gland during the CLND or the incidental removal of the normal parathyroid glands. In the literature, there are studies whose findings are correspond with our study.[17] The performing CLND increased the development of hypocalcaemia by 1.51-fold in the study of Duclos A et al,[6] by 1.56-fold in the study of Cho JN et al[7] and by 2.84-fold in the study of Docimo G et al.[9] In the study of Wang TX et al,[29] the performing central lymph node dissection increased the transient hypocalcaemia by 2.36-fold and permanent hypocalcaemia by 5.22-fold. When all risk factors were evaluated, the most risky factor causing postoperative hypocalcaemia was found to be CLND in our study.

Re-operative thyroid surgery is a procedure complicated by distorted anatomy and post-operative tissue changes. There are many studies that re-operative thyroid surgery as a risk factor for the development of hypocalcaemia.[17]

Cappellani A et al[30] reported that the frequency of transient hypocalcaemia was not affected in patients re-operated due to recurrent goitre, whereas permanent hypocalcaemia was found to be more frequent. In the studies of Hardman JC et al[31] and Pironi D. et al,[32] the development of hypocalcaemia was higher in patients re-operated due to recurrent goitre but this finding was not statistically significant in parallel with the results of our study.

4.1. Limitations of the study

The number of patients in the risk group was lower than the control group and some of our patients' data could not be reached due to the retrospective nature of our study. This reduced the statistical power of our study. Also, the estimation of preoperative serum iPTH and vitamin D levels are not performed routinely at our institution because of the concern of additional costs, which was considered only in symptomatic patients. CLND was the strongest predictor according to our study in terms of hypocalcaemia. Given that the parathyroid glands are damaged, we think that preoperatif vitamin D levels may not affect the accuracy of outcome in patients with CLND, because PTH is an important facilitator of the renal conversion of 25-hydroxyvitmain D to 1,25-dihydroxyvitamin D (calcitriol).

The patients included in the study represent a very heterogeneous group such as gender, benign-malignant diseases, extent of the surgical field, anatomical differences of the thyroid gland. Because of this heterogeneity, it is expected that the results of the present study show difference from the data of literature. We were able to access 381/818 patients with weight data, which could cause some bias.

5. Conclusion

The risk of postoperative hypocalcaemia increases in parallel with the size of the thyroid gland and CLND. Especially in patients who are female and have thyroid glands with substernal localization, the risk of developing postoperative hypocalcaemia may be predicted according to the extent of the surgery that will be planned before the operation. The postoperative findings of patients occurred due to hypocalcaemia may be reduced after the operation by determining the predisposing factors for hypocalcaemia and their effects and by taking necessary measures before the surgery. In this way, it may be provided that patient comfort is increased and the length of stay in hospital and cost are reduced.

Conflict of interest

All authors declare that we have no financial or non-financial conflicts of interest related to the subject matter or materials discussed in this article.

References

1. Bhattacharyya N, Fried MP. Assessment of the morbidity and complications of total thyroidectomy. *Arch Otolaryngol Head Neck Surg*. 2002;128(4):389—392.
2. Moulton-Barrett R, Crumley R, Jalilie S, et al. Complications of thyroid surgery. *Int Surg*. 1997 Jan—Mar;82(1):63—66.
3. Edafe O, Antakia R, Laskar N, Uttley L, Balasubramanian SP. Systematic review and meta-analysis of predictors of post-thyroidectomy hypocalcaemia. *Br J Surg*. 2014 Mar;101(4): 307—320.
4. Sitges-Serra A, Ruiz S, Girvent M, Manjón H, Dueñas JP, Sancho JJ. Outcome of protracted hypoparathyroidism after total thyroidectomy. *Br J Surg*. 2010 Nov;97(11):1687—1695.
5. Yamashita H, Noguchi S, Murakami T, et al. Calcium and its regulating hormones in patients with graves disease: sex differences and relation to postoperative tetany. *Eur J Surg*. 2000 Dec;166(12):924—928.
6. Duclos A, Peix JL, Colin C, et al. Influence of experience on performance of individual surgeons in thyroid surgery: prospective cross sectional multicentre study. *BMJ*. 2012 Jan 10; 344:d8041.
7. Cho JN, Park WS, Min SY. Predictors and risk factors of hypoparathyroidism after total thyroidectomy. *Int J Surg*. 2016 Oct; 34:47—52.
8. Luo H, Yang H, Zhao W, et al. Hypomagnesemia predicts postoperative biochemical hypocalcemia after thyroidectomy. *BMC Surg*. 2017 May 25;17(1):62.
9. Docimo G, Ruggiero R, Casalino G, Del Genio G, Docimo L, Tolone S. Risk factors for postoperative hypocalcemia. *Updates Surg*. 2017 Jun;69(2):255—260.
10. Eismontas V, Slepavicius A, Janusonis V, et al. Predictors of postoperative hypocalcemia occurring after a total thyroidectomy: results of prospective multicenter study. *BMC Surg*. 2018 Aug 9;18(1):55.
11. Kamer E, Unalp HR, Erbil Y, Akguner T, Issever H, Tarcan E. Early prediction of hypocalcemia after thyroidectomy by parathormone measurement in surgical site irrigation fluid. *Int J Surg*. 2009 Oct;7(5):466—471.
12. Lindblom P, Westerdahl J, Bergenfelz A. Low parathyroid hormone levels after thyroid surgery: a feasible predictor of hypocalcemia. *Surgery*. 2002 May;131(5):515—520.
13. Weiss A, Parina RP, Tang JA, Brumund KT, Chang DC, Bouvet M. Outcomes of thyroidectomy from a large California state database. *Am J Surg*. 2015 Dec;210(6):1170—1176. discussion 1176—7.
14. Hallgrimsson P, Nordenström E, Almquist M, Bergenfelz AO. Risk factors for medically treated hypocalcemia after surgery for Graves' disease: a Swedish multicenter study of 1,157 patients. *World J Surg*. 2012 Aug;36(8):1933—1942.
15. Bähler S, Müller W, Linder T, et al. Intraoperative parathyroid hormone measurement is the best predictor of postoperative symptomatic hypocalcemia. *HNO*. 2017 Dec;65(12):1000—1007.
16. Oltmann SC, Brekke AV, Schneider DF, Schaefer SC, Chen H, Sippel RS. Preventing postoperative hypocalcemia in patients with Graves disease: a prospective study. *Ann Surg Oncol*. 2015 Mar;22(3):952—958.
17. Caglià P, Puglisi S, Buffone A, et al. Post-thyroidectomy hypoparathyroidism, what should we keep in mind? *Ann Ital Chir*. 2017;6:371—381.
18. McHenry CR, Piotrowski JJ. Thyroidectomy in patients with marked thyroid enlargement: airway management, morbidity, and outcome. *Am Surg*. 1994 Aug;60(8):586—591.
19. Karabeyoglu M, Unal B, Dirican A, et al. The relation between preoperative ultrasonographic thyroid volüme analysis and thyroidectomy complications. *Endocr Regul*. 2009 Apr;43(2): 83—87.
20. Coimbra C, Monteiro F, Oliveira P, Ribeiro L, de Almeida MG, Condé A. Hypoparathyroidism following thyroidectomy: predictive factors. *Acta Otorrinolaringol Esp*. 2017 Mar — Apr; 68(2):106—111.
21. Ravikumar K, Muthukumar S, Sadacharan D, Suresh U, Sundarram T, Periyasamy S. The impact of thyroiditis on

morbidity and safety in patients undergoing total thyroidectomy. *Indian J Endocrinol Metab*. 2018 Jul—Aug;22(4):494—498.
22. Ozemir IA, Buldanli MZ, Yener O, et al. Factors affecting postoperative hypocalcemia after thyroid surgery: importance of incidental parathyroidectomy. *North Clin Istanb*. 2016 Apr 7;3(1):9—14.
23. Padur AA, Kumar N, Guru A, et al. Safety and effectiveness of total thyroidectomy and its comparison with subtotal thyroidectomy and other thyroid surgeries: a systematic review. *J Thyroid Res*. 2016;2016:7594615.
24. Kul F, Kirdak T, Sarkut P, Ocakoglu G, Korun N. Can parathormon levels after ipsilateral lobectomy predict postoperative hypocalcemia in patients undergoing total thyroidectomy? *Am Surg*. 2017 Apr 1;83(4):421—427.
25. Donatini G, Castagnet M, Desurmont T, Rudolph N, Othman D, Kraimps JL. Partial thyroidectomy for papillary thyroid microcarcinoma: is completion total thyroidectomy indicated? *World J Surg*. 2016 Mar;40(3):510—515.
26. Testini M, Gurrado A, Avenia N, et al. Does mediastinal extension of the goiter increase morbidity of total thyroidectomy? A multicenter study of 19,662 patients. *Ann Surg Oncol*. 2011 Aug;18(8):2251—2259.
27. Moten AS, Thibault DP, Willis AW, Willis AI. Demographics, disparities, and outcomes in substernal goiters in the United States. *Am J Surg*. 2016 Apr;211(4):703—709.
28. Bove A, Di Renzo RM, D'Urbano G, et al. Preoperative risk factors in total thyroidectomy of substernal goiter. *Ther Clin Risk Manag*. 2016 Nov 28;12:1805—1809.
29. Wang TX, Yu WB, Ma X, Song YT, Zhang NS. Risk factors of hypoparathyroidism following total or near total thyroidectomy. *Zhonghua Wai Ke Za Zhi*. 2016 Mar 1;54(3):206—211.
30. Cappellani A, Zanghì A, Cardì F, et al. Total thyroidectomy: the first, the best. The recurrent goiter issue. *Clin Ter*. 2017 May—Jun;168(3):e194—e198.
31. Hardman JC, Smith JA, Nankivell P, Sharma N, Watkinson JC. Re-operative thyroid surgery: a 20-year prospective cohort study at a tertiary referral centre. *Eur Arch Oto-Rhino-Laryngol*. 2015 Jun;272(6):1503—1508.
32. Pironi D, Pontone S, Vendettuoli M, et al. Prevention of complications during reoperative thyroid surgery. *Clin Ter*. 2014;165(4):e285—e290.