Original Article / Çalışma - Araştırma

The effect of primary thyroid surgery on the morbidity of reoperative thyroid surgery

Yeniden yapılan tiroid cerrahisinin morbiditesi üzerinde ilk yapılan tiroid cerrahisinin etkisi

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Objectives: This study aims to investigate the effect of primary surgery on the morbidity of reoperative thyroid surgery.

Patients and Methods: Fifty-seven patients (14 male, 43 female; mean age 41 years; range 21 to 70 years), who underwent reoperative thyroid surgery in our clinic between January 2007 and January 2012 were retrospectively analyzed in terms of vocal cord paralysis, temporary or permanent hypoparathyroidism, and other complications. The patients were classified into two groups. The first group consisted of 42 completion thyroidectomy patients that had undergone the primary operation of unilateral total lobectomy + isthmusectomy in our clinic, whereas the second group consisted of 15 patients that had undergone bilateral subtotal or near total thyroidectomy in another center. Complication rates were compared between the groups.

Results: Complication rates were observed as permanent vocal cord paralysis in one patient (1.7%), permanent hypocalcemia in two patients (3.5%) and temporary hypocalcemia in four patients (7%). None of the patients had temporary vocal cord paralysis. The complications in the second group were significantly higher than the first group (p=0.021).

Conclusion: The minimal operation should be hemithyroidectomy (total lobectomy and isthmusectomy) to minimize the complications. This approach removes the need for the intervention to the previous surgery field during reoperative thyroid surgery.

Key Words: Hypocalcemia; thyroid cancer; thyroidectomy; vocal cord paralysis.

Amaç: Bu çalışmada yeniden yapılan tiroid cerrahisinin morbiditesi üzerinde ilk yapılan tiroid cerrahisinin etkisi araştırıldı.

Hastalar ve Yöntemler: Kliniğimizde, Ocak 2007 - Ocak 2012 tarihleri arasında yeniden tiroid cerrahisi uygulanan 57 hasta (14 erkek, 43 kadın; ort. yaş 41 yıl; dağılım 21-70 yıl), retrospektif olarak vokal kord paralizisi, geçici veya kalıcı hipoparatiroidizm ve diğer komplikasyonlar açısından değerlendirildi. Hastalar iki grupta sınıflandırıldı. İlk grubu; kliniğimizde primer ameliyatı tek taraflı total lobektomi + istmusektomi olan 42 tamamlayıcı tiroidektomi hastası oluştururken, ikinci grubu farklı merkezlerde iki taraflı subtotal veya totale yakın tiroidektomi olan 15 hasta oluşturdu. Gruplar arasında komplikasyon oranları karşılaştırıldı.

Bulgular: Komplikasyon oranları, bir hastada (%1.7) kalıcı vokal kord paralizisi, iki hastada (%3.5) kalıcı hipokalsemi, dört hastada (%7) ise geçici hipokalsemi olarak gözlendi. Hastaların hiçbirinde geçici vokal kord paralizisi gözlenmedi. İkinci gruptaki komplikasyon oranlarının ilk gruptan anlamlı derecede yüksek olduğu gözlendi (p=0.021).

Sonuç: Komplikasyonları minimize etmek için minimal ameliyat hemitiroidektomi (total lobektomi ve istmusektomi) olmalıdır. Bu yaklaşım, yeniden yapılan tiroid cerrahisi esnasında aynı bölgeye tekrar cerrahi girişim ihtiyacını ortadan kaldırır.

Anahtar Sözcükler: Hipokalsemi; tiroid kanseri; tiroidektomi; vokal kord paralizi.

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The excision of the remaining lobe in patients that had previously undergone unilateral lobectomy is defined as "completion thyroidectomy" whereas surgical intervention performed for excision of residual thyroid tissue in patients that had previously undergone subtotal thyroid gland resection is termed "revision thyroidectomy" or "secondary thyroidectomy". However, all secondary interventions performed on patients who had previously undergone thyroid surgery are also termed "reoperative thyroid surgery (RTS)".[1,2]

Reoperative thyroid surgery is rarely performed for thyroid diseases. Reoperative thyroid surgery is generally used for nodular recurrences, previous incomplete thyroidectomies (such as nodulectomy, subtotal lobectomy or subtotal thyroidectomy), local recurrence of differentiated thyroid carcinomas, paratracheal and lateral nodal recurrences, and cases with recurrent hyperthyroidism despite the previous surgical intervention. In cases for revision, the anatomical variations caused by the fibrosis and scars that develop secondary to the previous operation pose higher risks to the laryngeal nerves and parathyroid glands.[3-5] Therefore, maneuvers that would not make the secondary operation difficult should be preferred during the primary operations, and the probability of a second operation should always be kept in mind. The control and management of recurrence after RTS is difficult and the mortality is high.[6] Reoperative thyroid surgery is a compelling and high risk intervention even for experienced surgeons.

The aim of this study is to determine the risk factors that increase morbidity for reoperative thyroid surgery and also to investigate the effect of primary thyroid surgery on this morbidity. Therefore we retrospectively reviewed our patients records who had undergone reoperative thyroid surgery.

PATIENTS AND METHODS

The records of 57 patients (14 males, 43 females; mean age 41 years; range 21 to 70 years) who had undergone RTS between January 2007 and January 2012 were retrospectively reviewed. The age, sex, indications for RTS, pathologic findings and complications were recorded. The pathological slides of patients that had undergone the primary operation in another center were obtained and re-evaluated by the pathology department in our hospital.

The patients were classified into two groups. The first group consisted of 42 completion thyroidectomy patients that had undergone the primary operation of unilateral total lobectomy + isthmusectomy in our clinic, whereas the second group consisted of 15 patients that had undergone bilateral subtotal or near total thyroidectomy in another center.

Statistical analysis

The categorical variables between group 1 and group 2 were analyzed by using the Chi square test or Fisher's exact test. Values of $p<0.05$ were considered statistically significant. The results are reported as number (n) and percent (%). Statistical analyses were performed using the SPSS (SPSS Inc., Chicago, Illinois, USA) for Windows version 18.0 statistical package program.

RESULTS

Preoperative diagnoses of 57 patients were as follows: 41 patients had papillary carcinoma, 10 patients had follicular carcinoma, one patient had medullary carcinoma and five patients had nodular goiter (Table 1). When the postoperative specimens of 41 patients with the preoperative diagnosis of papillary thyroid carcinoma were examined, 18 had nodular goiter, two had normal thyroid tissue, 16 had papillary carcinoma and five had Hashimoto's thyroiditis. The pathological reports of 10 patients with the preoperative diagnosis of follicular carcinoma revealed normal thyroid tissue in four patients, nodular goiter in four patients, follicular carcinoma in one patient, and Hurthle cell carcinoma in one patient after RTS. Of five patients with the diagnosis of nodular goiter preoperatively, four had nodular goiter and one had follicular adenoma postoperatively. The pathological report of a patient that underwent RTS with the diagnosis of medullary carcinoma also revealed medullary carcinoma after RTS. Two patients underwent neck dissection in the same session with RTS. One of them had papillary carcinoma, and other had medullary carcinoma.

The histopathological examination of the specimens following RTS revealed that malignant tumor was determined in 19 patients (33.3%), of which papillary carcinoma accounted for the majority (Table 1).

In the second group, three patients with the diagnosis of differentiated thyroid carcinoma had undergone RTS with the collaboration of the nuclear medicine department providing intraoperative gamma probe guidance in order to recognize the residual thyroid tissue easily. Reoperative thyroid surgery was performed either within the first week after the primary surgery or after a period of three months.

Patients that had undergone RTS were hospitalized for four to seven days. The serum calcium concentration and hypoparathyroidism clinical symptoms were assessed in the first 72 hours postoperatively. If there was any sign of hypoparathyroidism, calcium and vitamin D replacement therapy were given. The patients were followed by the endocrinology department for the regulation of calcium levels. The calcium replacement of the patients was decreased gradually after the 15th postoperative day. The serum calcium concentration was assessed for dose adjustment periodically. Symptomatic hypocalcemia was defined as serum calcium levels less than 2 mmol/l with clinical findings of carpopedal spasms or tingling or numbness of the extremities. If symptomatic hypocalcemia persisted beyond six months, permanent hypoparathyroidism was diagnosed.

Calcium levels were within the normal ranges in the preoperative serum samples, and the mean preoperative calcium level was determined to be 8.20 mg/dl. Postoperative calcium levels revealed that four patients (7%) had temporary hypocalcaemia, whereas two (3.5%) had permanent hypocalcaemia. In the first group (n=42), only one patient had permanent (2.3%) and one patient had temporary hypocalcaemia (2.3%). However, in the second group (n=15) three (20%) patients had temporary hypocalcaemia and one (6.6%) patient had permanent hypocalcaemia (Table 2). Temporary hypocalcaemia returned to the normal levels within 20 to 30 days.

All patients underwent vocal cord examination both preoperatively and postoperatively, and their calcium levels were measured preoperatively. Moreover, routine nerve monitoring was also used for the patients in the second group. Nerve integrity monitoring (NIM)-2 electromyographic system (Medtronic ENT, Jacksonville, FL, USA) was used for laryngeal nerve monitoring. The recurrent laryngeal nerve and parathyroid glands were planned to be identified and preserved. Parathyroid glands that had been suspected to be devascularized were evaluated via frozen section and implanted into the sternocleidomastoid muscle if the parathyroid tissue was identified. Thyroidectomy specimens were sent to the pathology department. Preoperative and postoperative pathological results of the patients were compared. The drains that had been routinely placed into the surgical site were removed after 24 to 72 hours. Temporary vocal cord paresis was defined as impaired mobility that resolved within six months and was considered permanent if persisted longer than six months.

While preoperative unilateral vocal cord paralysis was present in two of 57 patients before RTS, unilateral vocal cord paralysis was detected

Table 1. Preoperative and postoperative histopathological diagnosis of the patients

First thyroid surgery	n	%	Second thyroid surgery	n	%
Papillary carcinoma	41	71.99	Nodular goiter	18	31.5
			Papillary carcinoma	16	28
			Hashimoto's thyroiditis	5	8.7
			Normal thyroid tissue	2	3.5
Follicular carcinoma	10	17.5	Normal thyroid tissue	4	7
			Nodular goiter	4	7
			Follicular carcinoma	1	1.7
			Hurtle cell carcinoma	1	1.7
Nodular goiter	5	8.7	Nodular goiter	4	7
			Follicular adenoma	1	1.7
Medullar carcinoma	1	1.7	Medullar carcinoma	1	1.7

Table 2. Complication rates

	Group 1 (n=42)		Group 2 (n=15)		
	n	%	n	%	*p*
Complication					
No	40	–	10	–	
Yes	2	4.7	5	33.3	0.021
Type of complication					
Temporary hypocalcemia	1	2.3	3	20	
Permanent hypocalcemia	1	2.3	1	6.6	
Temporary RLN paralysis	–	–			
Permanent RLN paralysis	–	–	1	6.6	

Group 1: The patients that had undergone lobectomy+istmusectomy in our clinic as the primary operation; Group 2: The patients that had undergone bilateral subtotal thyroidectomy as the primary operation in a different center; RLN: Recurrent laryngeal nerve.

in one more (1.7%) patient after RTS. There was no vocal cord paralysis prior to the RTS in the first group, whereas two of 15 patients in the second group had unilateral vocal cord paralysis prior to the RTS. Postoperative vocal cord paralysis was determined in none of the patients in the first group, whereas postoperative unilateral vocal cord paralysis was determined in one (6.6%) of the patients in the second group (Table 2). In one-year follow-up, no improvement was observed regarding vocal paralysis in three patients and considered as permanent.

A significant difference in complication rates was shown between group 1 and group 2. The complications in group 2 were significantly higher than in group 1 (p=0.021).

DISCUSSION

Many surgeons and endocrinologists recommend total thyroidectomy for the treatment of well-differentiated thyroid carcinomas. However, well-differentiated thyroid carcinomas may not be detected until the definite diagnosis is made via the serial sections of excised thyroid tissue. For this reason, many surgeons limit the primary operation with lobectomy + isthmusectomy, and then suggest RTS (completion total thyroidectomy) in reference to the definite pathological outcome.[4] Because of higher complication risks of RTS, RAI (radioactive iodine) ablation therapy may be considered as an alternative therapy. However, it is well known that iodine uptake capacity of normal thyroid tissue is higher than that of the malignant tissue. Therefore, high dose recurrent ablation therapy is required for the huge residual thyroid tissues. It has been reported that RAI may cause problems such as radiation thyroiditis (pain, edema and thyrotoxicosis), as well as parathyroid injury, leukemia and pulmonary fibrosis particularly with high dose and long-term therapies.[4,7]

Recognizing and sparing the recurrent laryngeal nerve (RLN) is the critical issue during RTS. Identification of the RLN may be difficult because of the change in localization of the nerve or wound scarring and contracture. No temporary vocal cord paralysis was detected in this present study. However, unilateral permanent vocal cord paralysis developed in one patient (1.7%). Preoperative laryngoscopic evaluation revealed unilateral vocal cord paralysis in two patients of the second group. In the study performed by Beahrs and Vandertoll[8] in 1963, RTS had been performed on 548 patients and the incidence of vocal cord paralysis was reported to be 17%. The complication rates have decreased in years with the increase in experiences and technical equipment. In studies regarding the complication rates seen after RTS, the rate of temporary recurrent nerve injury changes from 0 to 10%, whereas the rate of permanent recurrent nerve injury changes from 0 to 6% (Table 3). The difference between the rates in the literature might have resulted from the inadequate preoperative and postoperative vocal cord examination. Furthermore, there is no information in the literature whether the vocal cord paralysis was unilateral or bilateral. In fact, unilateral or bilateral vocal cord paralysis makes substantial differences for treatment in the postoperative period. In some studies, it has been reported that vocal cord examination was performed only

Table 3. Complication rates seen after reoperative thyroid surgery

		Hypoparathyroidism		Recurrent nerve injury	
	Number of cases	Temporary (%)	Permanent (%)	Temporary (%)	Permanent (%)
Chao et al.[4]	115	5.2	1.7	2.6	1.7
Eroğlu et al.[7]	165	‡	‡	3	5.5
Lefevre et al.[9]	460	6.3	2.4	1.1	1.7
Pasieka et al.[10]	47	8.0	1.7	5.0	0
Calabro et al.[3]	66	12.1	0	1.5	0
Glockzin et al.[11]	128	7.0	3.1	6.2	3.1
Seiler et al.[12]	166	‡	‡	‡	5.6
Terris et al.[13]	42	4.5	0	0	0
Present study	57	7	3.5	0	1.7

‡ Referanslarda ilgili bilgi bulunmamaktadır.

in symptomatic patients.[9] Bilateral vocal cord paralysis may require tracheostomy because of respiratory distress. However, unilateral vocal cord paralyses are sometimes asymptomatic and may be missed unless a laryngoscopic evaluation is made routinely before and after surgery.

The other significant complication is permanent hypoparathyroidism. In this study, the rates of temporary and permanent hypoparathyroidism were determined to be 7% and 3.5% respectively. The incidence of temporary hypoparathyroidism in the literature changes from 3 to 15%, whereas the incidence of permanent hypoparathyroidism is lower after RTS (Table 3).[3,4,7,9,10-13]

The best way to reduce the rate of complications in RTS is the choice of proper surgical intervention during the primary operation.[1] For this reason, the patient should be well evaluated before the first operation and the indication for the operation should accurately be assessed. Hemithyroidectomy (total lobectomy and isthmusectomy) should be the minimal operation in thyroid surgery. This kind of approach removes the need for second operation on the operated side. The probability of a second surgical intervention should always be kept in mind during the first operation. Performing nodule excision or subtotal thyroidectomy during the first operation may risk the identification of both RLN and parathyroid glands during the RTS performed on the same lobe. In this study, it was observed that the complication rates were higher in the second group (Table 2). The patient who developed permanent vocal cord paralysis had undergone subtotal thyroidectomy in another center. There is no other study that compares the complication rates between the patients that had undergone lobectomy + isthmusectomy as the primary operation and those that had undergone bilateral subtotal thyroidectomy as the primary operation.

There is controversy regarding the timing of RTS in the literature. Edema, hemorrhage, scar, inflammation can make early RTS dangerous. In order to decrease the incidence of complications, RTS should be performed either within the seven days after primary surgery or after a period of three to four months.[3,14] Chao et al.[4] performed RTS in only nine of 50 patients either within the first seven days or after three months. They observed no difference regarding complication rates when compared with the remaining patients. In our series, RTS was performed either within the first seven days after the primary surgery or after a period of three months.

Intraoperative nerve monitoring which is the gold standard for the identification of RLN plays an important role in high risk operations such as RTS. This is the gold standard for the identification of RLN.[15] However different approaches have been defined in the literature for the identification of RLN during the operation (lateral-inferior-superior). Lefevre et al.[9] recommends the lateral approach since the exposure of the superior pole of the thyroid gland and the preservation of the superior parathyroid gland is better. On the other hand, Richer and Wenig[16] prefers the inferior approach. However, it has been emphasized in the literature that the most appropriate approach would be the choice of the identifiable anatomical structures in the non-dissected areas via the

experience of the surgeon and the evaluation of each patient individually.[16]

Preservation of the parathyroid glands is of great importance to avoid hypoparathyroidism and the identification of the glands may be difficult in RTS because of the fibrosis around the vascular pedicle. It has been suggested that the preservation of the vascular pedicle and a capsular dissection preserves the adequate blood supply for the gland.[2] During the operation, parathyroid glands may be devascularized due to excessive manipulation or hematoma. Careful dissection and over manipulation should be avoided, and superior and inferior thyroid arteries should be dissected close to the thyroid gland. If considered devascularized, parathyroid glands should be implanted into the opposite sternocleidomastoid muscle,[6] trapezius muscle or into the forearm.

Even in benign thyroid disease, subtotal thyroid lobectomy should not be done. If the histopathological findings reveal differentiated thyroid carcinoma, the residual thyroid tissue may be excised by considering the risk groups of the patients. In these cases, since the normal tissue planes could not be differentiated because of scar and fibrosis, it is quite difficult to expose and completely remove residual thyroid tissue. To find the residual thyroid tissue easily and decrease the complication risks in the patient a gamma probe can be used intraoperatively. Although the gamma probe is generally used for the parathyroid diseases, some surgeons use it in RTS, thus, maximal resection is achieved.[17,18] We know that the volume of the residual thyroid tissue is the most significant factor that affects the success of RAI therapy in the differentiated thyroid carcinomas, and these tissues can be found easily by the assistance of gamma probe and greater thyroid tissue can be excised, so the chance for ablation with RAI therapy is increased. In our clinic, gamma probe guided RTS was performed in three patients who had undergone bilateral subtotal thyroidectomy in another center and whose histopathological findings revealed differentiated thyroid carcinoma. Thus, residual thyroid tissue which is difficult to recognize under normal conditions in the scar tissue, was exposed more easily and it was decided that use of the gamma probe is quite beneficial.

In conclusion, patients should be carefully evaluated prior to RTS and if the patients do not have definite indication for surgery should be followed with non-surgical treatments. If RTS is required, the operation should be performed by experienced surgeons to decrease the complication risks. The minimal operation in thyroid surgery should be hemithyroidectomy (total lobectomy and isthmusectomy). This approach removes the need for intervention on the previously operated field when performing RTS. The probability for the second surgical intervention should always be kept in mind during the first operation. In order to minimize the complications and enhance the success of the operation, diagnostic methods such as fine needle aspiration cytology, computed tomography, scintigraphy and ultrasonography could be used before surgery. Monitoring of the recurrent laryngeal nerve, intraoperative use of a gamma probe, and obtaining tissue diagnosis via frozen section examination may not only help avoid the incidence of complications during RTS but may also prevent further surgeries in the future.

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