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Original Article

Comparison of Indications and Complications in Patients Undergoing Primary and Reoperative Thyroid Surgery

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ABSTRACT

Objective: Today, indications for thyroid surgery have significantly narrowed. Factors such as the increase in the number of experienced cytopathologists, the performance of biopsies by clinicians, and the significantly improved evaluation of ultrasound have contributed to this. Due to the increased reliability of needle aspiration biopsies, multiple biopsies can be performed, especially in patients with indications for re-operative surgery, and many patients can avoid re-operative surgery. We aimed to investigate the indications for re-operative thyroid surgery in our clinic by evaluating the pathology results and complications of patients who underwent re-operative thyroid surgery.

Methods: Primary (primary group) and re-operative thyroid patients (re-operative group) who underwent surgery in the Breast and Endocrine Surgery Unit of our hospital's General Surgery Clinic between February 2014 and August 2019 were included in the study. Patient characteristics and demographics, primary surgery, type of re-operative surgery, indication for primary surgery, indication for re-operative surgery, operation time, perioperative complications, and postoperative complications were used as evaluation parameters.

Results: 934 patients (93.6%) in the primary group and 64 patients (6.4%) in the re-operative group were compared in accordance with the study criteria. No significant differences were found in postoperative voice findings and vocal cord paralysis, while preoperative and postoperative hypocalcemia findings were significantly more common in the re-operative group across multiple criteria ($p<0.05$).

Conclusion: Indications and pathological examination results for primary and re-operative thyroid patients are similar according to current guidelines. While this reflects the accuracy of the indications, the high rates of hypocalcemia and persistent hypoparathyroidism in the re-operative patient group necessitate the restriction of indications. Prospective studies are needed for patients with narrower indications.

INTRODUCTION

In recent years, the indications for thyroid surgery have significantly narrowed. This has been attributed to several factors, including the addition of diagnoses such as Non-Invasive Follicular Thyroid neoplasm with Papillary-like nuclear features (NIFT-P) to recent guidelines, the increase in the number of experienced cytopathologists, the performance of biopsies by shortage, and the substantial improvement in the use of ultrasonography for evaluation.[1,2] Despite these advances, the number of thyroid cancer surgeries has proportionally increased. Furthermore, a rise in aggressive variants of papillary carcinoma and an increased incidence of papillary carcinoma in younger populations have led to a higher mortality rate from thyroid cancer.[3]

In our country, as in the current ATA (American Thyroid Association) guidelines, the 2020 Thyroid Diseases Guideline published by the Turkish Society of Endocrinology and Metabolism does not include subtotal or near-total thyroidectomy procedures.[4] However, due to the widespread use of tissue-preserving surgeries up to 15 years ago, there is still a need for completion thyroidectomies.[5] Additionally, incomplete surgeries (such as missed mediastinal thyroid tissue), the necessity of lymph node dissections in thyroid cancers, or cases where the thyroid bed has been reopened for other reasons (such as extensive parathyroid exploration, esophageal surgery, or inadvertent entry into the thyroid bed during anterior cervical stabilization leading to iatrogenic thyroid injury) may require re-operative thyroid surgery. Like all secondary operations, re-operative thyroid surgery presents significant challenges. In particular, surgical adhesions around the recurrent laryngeal nerve, difficulties in identifying the parathyroid glands, and the risk of developing hypoparathyroidism can make these procedures highly demanding.[6]

Due to the increased reliability of fine-needle aspiration biopsies, multiple biopsies can be performed, particularly in patients considered for re-operative surgery, and most patients can thus be spared from reoperation. However, in patients whose cytology results include nondiagnostic material, atypia of undetermined significance, or follicular lesion of undetermined significance, the fact that postoperative pathological findings after repeated biopsies tend to favor benign pathologies according to guideline recommendations is noteworthy.[7]

The aim of this study is to evaluate the pathological results and complications of patients who underwent re-operative thyroid surgery in a high-volume center and to question the indications for such surgeries. By comparing the findings obtained in our clinical practice with the indications recommended by current guidelines, we aim to provide further data on the necessity of re-operative surgery and to shed light on future research in this field. In addition, by sharing our experience regarding postoperative complications and surgical challenges, we aim to contribute to the development of a more selective and effective approach to re-operative thyroid surgery.

MATERIALS AND METHODS

This study was designed as a retrospective analysis and conducted between February 2014 and August 2019 in the Breast and Endocrine Surgery Unit of the Department of General Surgery at our hospital. The study included patients who underwent either primary thyroid surgery (first surgical intervention) or re-operative thyroid surgery (patients with a previous thyroid operation requiring a second surgical procedure). Patients were divided into two groups: The Primary Group, consisting of patients who underwent thyroid surgery for the first time, and the Re-operative Group, consisting of patients who had previously undergone thyroid surgery and required a second surgical intervention.

Patients who underwent unilateral lobectomy without a surgical procedure on the contralateral lobe (i.e., lobectomy followed by completion thyroidectomy) were excluded, as surgical standardization could not be achieved in this group. Additionally, patients who were not followed up for at least one year after surgery or for whom permanent hypoparathyroidism could not be assessed were excluded from the study. Patients who failed to complete the required follow-up examinations or whose data were insufficient were also excluded from the analysis.

Demographic and clinical characteristics of the patients, types of primary and re-operative surgery, indications for both procedures, operative time, and intraoperative and postoperative complications were evaluated. All data were collected from the hospital database. Ethical approval for the study and data collection process was obtained from the Kartal Dr. Lütfi Kırdar Hospital Ethics Committee (Date: 25/09/2019, Approval No: 2019/514/162/2). All procedures were conducted in accordance with the principles of the Declaration of Helsinki.

Statistical Analysis

Study data were analyzed using descriptive statistical methods (mean, standard deviation, frequency, percentage, minimum, and maximum values). The distribution of variables between groups was assessed for normality using the Shapiro-Wilk test. For normally distributed quantitative variables, comparisons between two groups were performed using the independent samples t-test. Quantitative variables that did not follow a normal distribution were analyzed using the Mann-Whitney U test. Categorical variables were compared using the Pearson chi-square test or Fisher's exact test when appropriate. For multiple comparisons, the Bonferroni correction was applied. A p-value<0.05 was considered statistically significant.

RESULTS

Between February 2014 and August 2019, a total of 1,500 thyroid surgeries were performed in our clinic (Fig. 1). Of these patients, 1,321 (88.1%) underwent their primary surgery, while 179 (11.9%) underwent a re-operative procedure at our clinic. After excluding patients who underwent lobectomy-completion thyroidectomy, 998 patients meeting the study criteria were included. In the Primary group, 934 patients (93.6%) and in the Re-operative group, 64 patients (6.4%) were compared according to the study criteria.

The mean age in the Primary group was 50.8±12.9 years, and in the Re-operative group, it was 50.5±13.5 years, with no statistically significant difference between the groups (Fig. 2). In the Primary group, 717 patients (76.8%) were female, while in the Re-operative group, 56 patients (87.5%) were female. The proportion of female patients was significantly higher in the Re-operative group compared to the Primary group ($p<0.05$).

The distribution of surgical indications for patients in the Primary and Re-operative groups is shown in Table 1. The most common indication in all groups was compressive symptoms, and no significant difference in surgical indications was observed between the groups ($p>0.05$).

Preoperative evaluation of patients' calcium levels and thyroid function tests is presented in Table 2. There was a

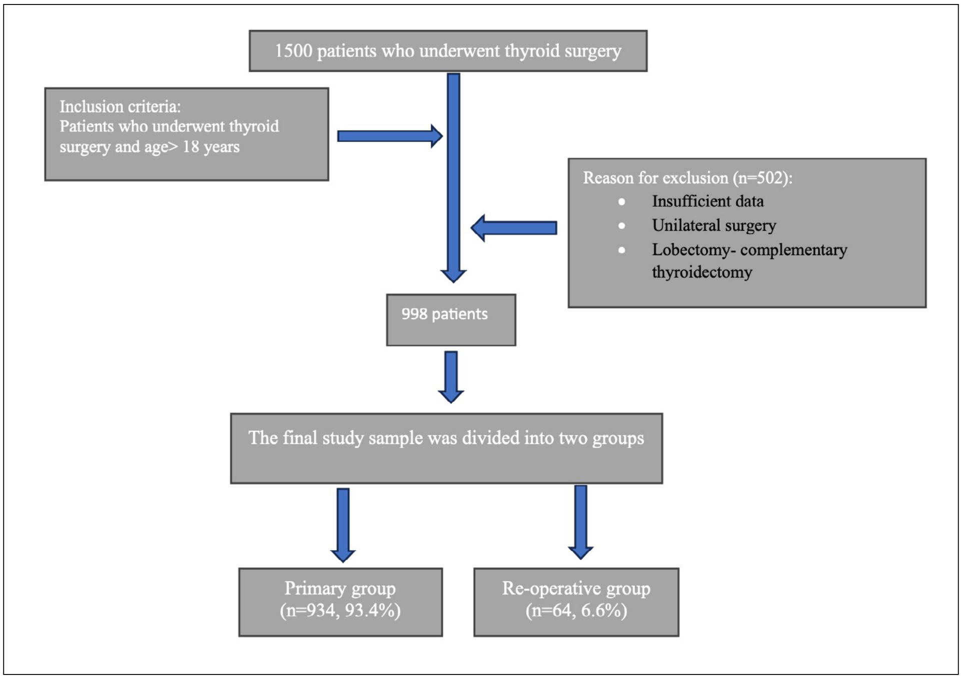

Figure 1. Flow chart of study population.

statistically significant difference between the two groups in terms of mean preoperative calcium levels (Fig. 3) ($p<0.001$). Additionally, statistically significant differences were observed between the groups regarding subclinical hyperthyroidism and subclinical hypothyroidism ($p<0.05$).

The distribution of surgical procedures in the Primary and Re-operative groups is presented in Table 3. Total thyroidectomy was the most commonly performed procedure in both groups, with a frequency comparable to that of total thyroidectomy combined with central neck dissection ($p>0.05$). However, it was performed significantly more often than other types of surgery ($p<0.05$).

Postoperative pathological results are presented in Table 4. The Primary and Re-operative groups showed similar pathological outcomes ($p>0.05$).

Voice hoarseness complications are presented in Table 5. The proportion of patients without voice/vocal cord pathology was significantly lower in the Re-operative group ($p<0.05$). Additionally, preoperative unilateral vocal cord paralysis was significantly more common in the re-operative group ($p<0.05$). However, postoperative voice hoarseness, independent of vocal cord paralysis, was ob-

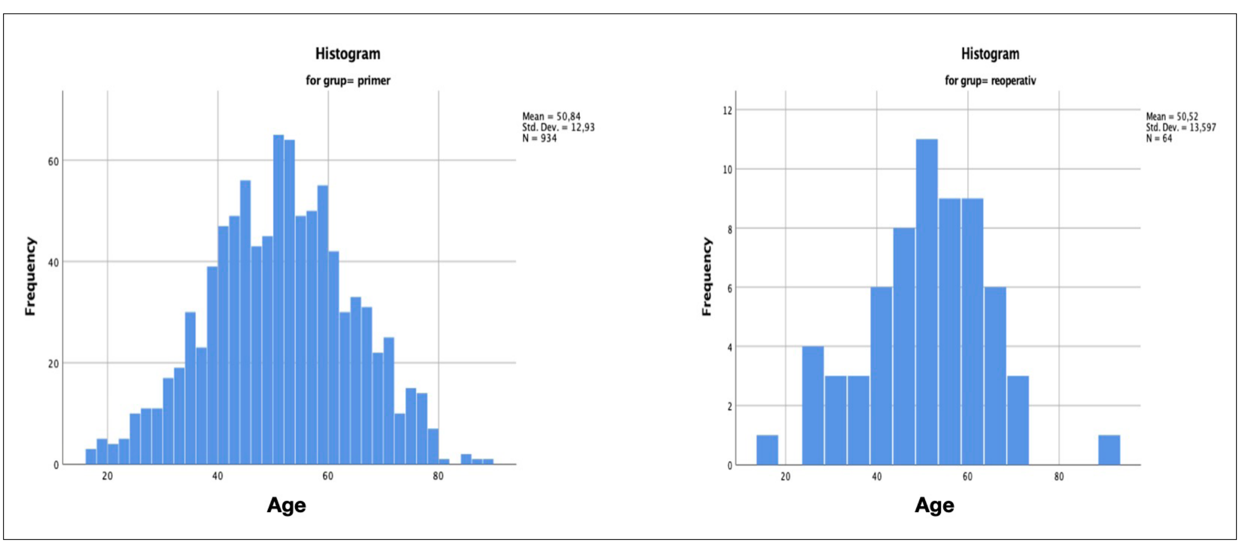

Figure 2. Age distribution of study population.

Table 1. Distribution of surgical ındications in primary and re-operative groups

Surgical Indications	Primary (n=934, 93.6%)	Re-operative (n=64, 6.4%)
Compression Symptom, n (%)	267 (28.6%)	22 (34.4%)
Toxic MNG, n (%)	193 (20.7%)	5 (7.8%)
Papiller Carsinom, n (%)	113 (12.1%)	11 (17.2%)
Suspicion of malignancy, n (%)	93 (10%)	10 (15.6%)
AUS twice, n (%)	82 (8.8%)	8 (12.5%)
Graves, n (%)	68 (7.3%)	0
Hurthle Cell Neoplasia, n (%)	50 (5.4%)	3 (4.7%)
Follicular Neoplasia, n (%)	34 (3.6%)	3 (4.7%)
Recurrent Nondiagnostic, n (%)	32 (3.4%)	2 (3.1%)
Thyroiditis, n (%)	2 (0.2%)	0

MNG: Multinodular goiter; AUS: Atypia of undetermined significance.

Table 2. Calcium and thyroid hormone evaluations of patients

	Primary (n=934, 93.6%)	Re-operative (n=64, 6.4%)
Calcium (mg/dl), mean±SD	9.54±0.61	9.24±0.64
Euthyroid, n (%)	660 (70.7%)	50 (78.1%)
Hypothyroidism, n (%)	11 (1.2%)	2 (3.1%)
Hyperthyroidism, n (%)	45 (4.8%)	0
Subclinical hypothyroidism, n (%)	22 (2.4%)	8 (12.5%)
Subclinical hyperthyroidism, n (%)	196 (21%)	4 (6.3%)

SD: Standard deviation.

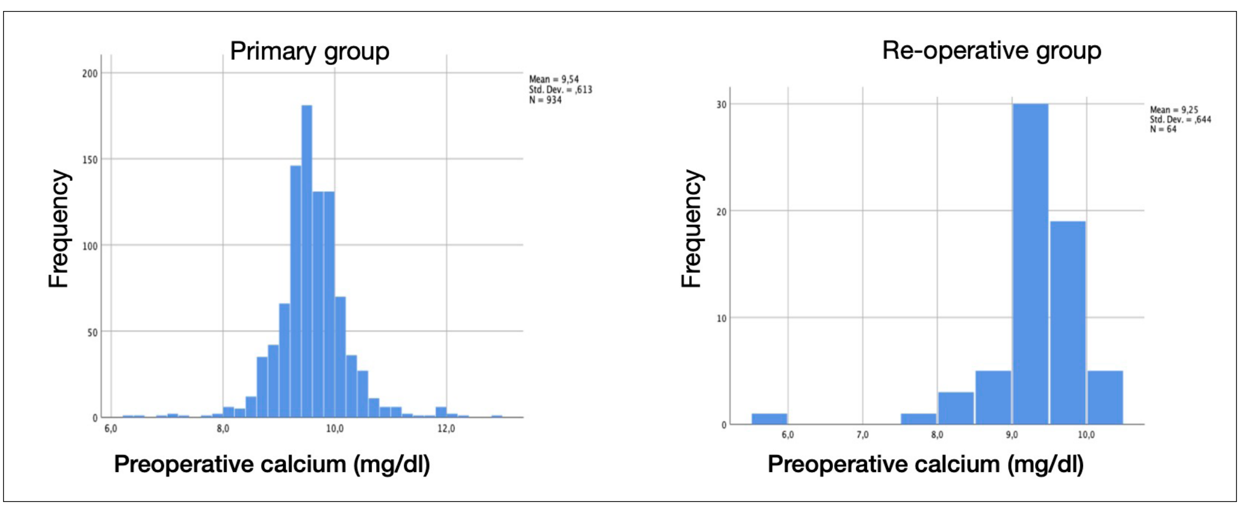

Figure 3. Preoperative mean calcium levels.

served at a similar rate in both groups. Although the only patient requiring tracheostomy was in the Primary group, there was no significant difference between the groups.

Postoperative bleeding findings are presented in Table 5. No statistically significant difference was observed between the two groups in terms of postoperative bleeding-related complications.

Postoperative hypocalcemia findings were evaluated according to biochemical parameters and are presented in Table 6. The number of patients with postoperative

Table 3. Surgery distribution of the groups

Type of Surgery	Primary (n=934, 93.6%)	Re-operative (n=64, 6.4%)
TT	894 (89.6%)	56 (5.6%)
TT+CCD	38 (3.8%)	5 (0.5 %)
TT+MRND	2 (0.2%)	2 (0.2%)
CCD	0	1 (0.1%)

TT: Total thyroidectomy; TT+CCD: Total thyroidectomy + central compartment dissection; TT+MRND: Total thyroidectomy + modified radical neck dissection; CCD: Central compartment dissection.

hypocalcemia was significantly higher in the Re-operative group ($p<0.05$). However, both groups were similar regarding patients with biochemical hypocalcemia without symptoms. Patients with hypocalcemia accompanied by low parathyroid hormone levels and clinical symptoms were significantly more frequent in the Re-operative group ($p<0.05$). Additionally, preoperative hypoparathyroidism was significantly more common in the Re-operative group ($p<0.05$).

The duration-based and permanent-versus-transient evaluation of hypocalcemia is presented in Table 6. The number of patients without hypocalcemia was significantly higher in the Primary group ($p<0.05$). Transient hypocalcemia lasting less than one month was significantly more frequent in the Re-operative group. Similarly, permanent hypoparathyroidism (>12 months) was significantly more common in the Re-operative group ($p<0.05$).

Table 4. Postoperative pathology results

	Primary (n=934, 93.6%)	Re-operative (n=64, 6.4%)
Benign, n (%)	513 (54.9%)	41 (64.1%)
Papillary Microcarcinoma, n (%)	190 (20.3%)	8 (12.5%)
Papillary Carcinoma, n (%)	213 (22.8%)	14 (21.9%)
Medullary Carcinoma, n (%)	6 (0.6%)	1 (1.6%)
Papillary + Medullary Carcinoma, n (%)	2 (0.2%)	0
NIFT-P, n (%)	6 (0.6%)	0
Poorly Differentiated Carcinoma, n (%)	4 (0.4%)	0

NIFT-P: Non-Invasive Follicular Thyroid Neoplasm with Papillary-like Nuclear Features.

Table 5. Hoarseness and postoperative bleeding

	Primary (n=934, 93.6%)	Re-operative (n=64, 6.4%)
No features, n (%)	898 (96.1%)	57 (89.1%)
Voice is hoarse, vocal cords are normal, n (%)	17 (1.8%)	2 (3.1%)
Hoarse voice, vocal cord paralysis, n (%)	16 (1.7%)	3 (4.7%)
Preop vocal cord paralysis (one side), n (%)	2 (0.2%)	2 (3.1%)
Tracheostomy, n (%)	1 (0.1%)	0
No Bleeding, n (%)	906 (97%)	61 (95.3%)
Bleeding Yes - bleeding control, n (%)	3 (0.3%)	1 (1.6%)
Bleeding Yes - conservative, n (%)	25 (2.7%)	2 (3.1%)

DISCUSSION

One of the key priorities in the treatment of thyroid diseases is to protect patients from unnecessary surgery. The risk-benefit relationship should be carefully evaluated, and a comprehensive treatment plan should be provided, reserving surgery only when indicated.[8] The aim of surgical treatment for thyroid diseases is to achieve the most effective treatment with the lowest complication and recurrence rates. Numerous risk factors influence complication rates, including surgeon experience, patient sex, previous thyroid surgery, and anatomical variations.

In patients with thyroid cancer, total thyroidectomy is considered the standard approach.[9] Advances in surgical technique, nerve monitoring, and the limitations of subtotal thyroidectomy have led to total thyroidectomy being increasingly preferred even for some benign thyroid

Table 6. Postoperative hypocalcemia

	Primary (n=934, 93.6%)	Re-operative (n=64, 6.4%)
None, n (%)	682 (73%)	34 (53.1%)
Biochemical hypocalcemia, symptoms (-), n (%)	103 (11%)	12 (18.8%)
Biochemical hypocalcemia, symptoms (+), n (%)	35 (3.7%)	3 (4.7%)
PTH low, hypocalcemia, symptom (-), n (%)	45 (4.8%)	5 (7.8%)
PTH low, hypocalcemia, symptom (+), n (%)	68 (7.3%)	9 (14.1%)
Preoperative hypoparathyroidism patient, n (%)	1 (0.1%)	1 (1.6%)
Temporary, <1 month, n (%)	164 (17.6%)	18 (28.1)
Temporary, 1-3 months, n (%)	49 (5.2%)	4 (6.3%)
Temporary, 3-6 months, n (%)	10 (1.1%)	2 (3.1%)
Temporary, 6-12 months, n (%)	10 (1.1%)	1 (1.6%)
>12 months, n (%)	19 (2.0%)	5 (7.8%)

PTH: Parathyroid hormone.

conditions. Successful hormone replacement therapy also supports the choice of total thyroidectomy.[10]

Today, total thyroidectomy allows radical surgical treatment without leaving any residual thyroid tissue, effectively eliminating the risk of recurrent disease. Cappellani et al.[11] noted that preventing recurrent goiter is best achieved through primary total thyroidectomy. Total thyroidectomy is a safe procedure with a low incidence of permanent complications, thereby reducing the need for secondary surgery.[12]

Historically, many surgeons preferred bilateral subtotal thyroidectomy to minimize operative risk and preserve a small portion of functioning tissue.[13] However, subtotal thyroidectomy carries a lifelong risk of recurrence in some patients. After subtotal resection of multinodular goiter, recurrence rates of up to 40% have been reported in long-term follow-up.[14]

Differences in perioperative complication rates cannot justify performing less than total thyroidectomy, even in benign disease. The morbidity associated with repeat surgery alone is a strong reason to avoid conservative procedures. Furthermore, suppressive therapy with levothyroxine often fails to prevent recurrence and may induce morbidity in some cases.[15] Surgical treatment of recurrent disease carries higher morbidity than primary total thyroidectomy.[11] Scar tissue and altered anatomy from previous surgery complicate dissection and increase complication risk in re-operative procedures.

In a study by Osmólski et al.[16] approximately 850 thyroidectomies were retrospectively reviewed, showing that re-operative thyroidectomies had significantly higher rates of temporary and permanent recurrent laryngeal nerve injury compared to primary surgeries. Rates of hypoparathyroidism were also significantly higher after reoperation.

To ensure homogeneity in our sample, we included only total thyroidectomy patients. Although the proportion of female patients in the Primary group was lower than in the Re-operative group, this is likely explained by the fact that the re-operative cohort consisted predominantly of female patients.

When comparing indications, compressive symptoms were the most frequent. This refers to nodules >4 cm or nodules <4 cm causing respiratory compromise on imaging. Similar indications in both groups reflect adherence to ATA and TEMD guidelines . Likewise, the lack of statistical difference in pathological outcomes between groups supports the accuracy of these indications. Rates of total thyroidectomy and total thyroidectomy with central compartment dissection were similar and significantly higher than other procedures, consistent with shared indications.

As expected, mean preoperative calcium levels were higher in the Primary group, largely due to heterogeneous distribution in the Re-operative group. Hypocalcemia and subclinical hypothyroidism were more frequent in the Re-operative group, likely due to reduced or nonfunctional residual tissue.[4] Conversely, subclinical hyperthyroidism was more common in the Primary group , reflecting residual tissue with normal or excessive function.

Early complications were evaluated separately from late complications. Postoperative bleeding was similar between groups with no statistical difference. Early hypocalcemia was defined as occurring within the first 24-72 hours postoperatively, potentially prolonging hospital stay if symptomatic.[17] Postoperative hypocalcemia was more frequent in the Re-operative group, particularly symptomatic patients with concurrent low parathyroid hormone and calcium levels. Within the first month, the incidence of hypocalcemia and permanent hypoparathyroidism was significantly lower in the Primary group.

The primary goals of this study were to compare indications and complication rates. The lack of difference in indications validates the implementation of current guidelines in our clinic following subspecialization in 2013. Subspecialization has likely contributed to the lower complication rates observed compared to historical data.[18] Although nerve monitoring is commonly used in current practice, its application during the study period was below 5%, limiting the assessment of its effect. The retrospective nature of the study is another limitation.

Despite similar indications, differences in complications were observed. The main complication remained calcium metabolism disturbances rather than vocal cord paralysis, even with limited nerve monitoring. As expected, the proportion of patients without preoperative voice or vocal cord pathology was lower, and the proportion with unilateral preoperative vocal cord paralysis was higher in the Re-operative group. Postoperative vocal cord paralysis and voice hoarseness were similar and low in both groups, likely due to increased surgical experience after subspecialization. However, experience alone did not reduce calcium metabolism complications.[18]

The higher rates of transient hypocalcemia and permanent hypoparathyroidism in the Re-operative group highlight the need to carefully evaluate surgical indications. Notably, 64.1% of re-operative patients had benign pathology. Patients with toxic goiter, compressive symptoms, repeated AUS, or recurrent nondiagnostic findings could be considered for alternative management such as radioactive iodine or repeat biopsy. Permanent hypoparathyroidism is difficult to manage, often inadequately treated, and significantly reduces quality of life. Its occurrence is largely unavoidable due to fibrosis and adhesions in re-operative fields and the low likelihood of preserving parathyroid function during surgery.[19]

Although recurrent laryngeal nerve preservation is enhanced by surgical expertise and stimulation techniques, parathyroid protection is not fully ensured.[20] Therefore, narrowing surgical indications in re-operative patients may reduce complication rates to levels similar to primary cases. Malignancy must still be excluded, which can often be achieved through repeat biopsies. The cumulative complication risk of multiple biopsies is likely lower than that of hypocalcemia. As subtotal or near-total thyroidectomies have been largely abandoned, the number of re-operative patients is gradually decreasing, and in the next 20 years, reoperation will primarily concern cancer recurrence.

Conclusion

Primary and re-operative thyroid patients show similar surgical indications and pathological outcomes when managed according to current guidelines. While this reflects the accuracy of the indications, the higher rates of hypocalcemia and permanent hypoparathyroidism in the re-operative group highlight the need to restrict surgical indications in these patients. Prospective studies are warranted to evaluate outcomes in patients managed with more selective, guideline-based indications.

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Ethics Committee Approval

The study was approved by the Ethics Committee of University of Health Sciences Türkiye, Kartal City Hospital (Date: 25.09.2019, Decision No: 514/162/2).

Informed Consent

Due to the retrospective design of our study, informed consent was not obtained.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: O.A., H.E.S.; Design: O.A., H.E.S, H.F.K.; Supervision: H.E.S., H.F.K; Materials: O.A., M.K.B.; Data collection &/or processing: O.A., M.K.B.; Analysis and/or interpretation: O.A., H.E.S.; Literature search: O.A., M.K.B., H.E.S.; Writing: O.A., H.E.S.; Critical review: H.E.S., H.F.K.

Conflict of Interest

None declared.

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Primer ve Re-operatif Tiroid Cerrahisi Uygulanan Hastaların Endikasyon ve Komplikasyonlarının Karşılaştırılması

Amaç: Günümüzde tiroid ameliyat endikasyonları belirgin olarak daralmıştır. Deneyimli sitopatolog sayısında artış, biyopsilerin klinisyenler tarafından yapılması, ultrasonografinin belirgin olarak daha iyi şekilde değerlendirmede yer alması gibi faktörler bu hususta rol oynamıştır. İğne aspirasyon biyopsilerinde güvenilirliğin artması nedeniyle özellikle re-operatif cerrahi endikasyonu konulacak hastalarda multipl biyopsiler yapılabilmekte ve çoğu hasta reoperatif cerrahiden korunabilmektedir. Kliniğimizde re-operatif tiroid cerrahisi uygulanan hastaların patoloji sonuçları eşliğinde komplikasyonları da değerlendirerek re-operatif tiroid cerrahisi endikasyonlarını sorgulamayı amaçladık.

Gereç ve Yöntem: Şubat 2014-Ağustos 2019 tarihleri arasında hastanemizin Genel Cerrahi Kliniği Meme ve Endokrin Hastalıkları Cerrahisi Birimi' nde ameliyat edilen primer (Primer grup) ve re-operatif tiroid hastaları (Re-operatif grup) çalışmaya dahil edilmiştir. Hastaların karakteristik ve demografik özellikleri, primer ameliyat, re-operatif cerrahi tipi, primer cerrahi endikasyonu, re-operatif cerrahi endikasyonu, operasyon süresi, peroperatif komplikasyonlar, postoperatif komplikasyonlar değerlendirme parametreleri olarak işleme alınmıştır.

Bulgular: Primer grupta 934 (%93.6), re-operatif grupta ise 64 (%6.4) hasta çalışma kriterleriyle uyumlu olarak karşılaştırıldı. Postoperatif ses bulguları ve vokal kord paralizisi açısından anlamlı farklılık saptanmazken, preoperatif ve postoperatif hipokalsemi bulguları pek çok kriter değerlendirmesinde re-operatif grupta anlamlı olarak daha fazla saptandı ($p<0.05$).

Sonuç: Primer ve re-operatif tiroid hastaları güncel kılavuzlar eşliğinde endikasyonları ve patolojik inceleme sonuçları benzerlikler göstermektedir. Bu durum endikasyonların doğruluğunu yansıtmakla beraber re-operatif hasta grubunda hipokalsemi ve kalıcı hipoparatiroidi oranının yüksek olması nedeniyle re-operatif hasta grubunda endikasyon kısıtlamasının gerekliliği söz konusudur. Endikasyonların daraltılarak takip edildiği hastalarla ilgili prospektif çalışmalara ihtiyaç vardır.

Anahtar Sözcükler: Hipokalsemi; hipoparatiroidi; total tiroidektomi; vokal kord paralizisi.