

Thyroidectomy for the Management of Differentiated Thyroid Carcinoma and their Outcome on Early Postoperative Complications: A 6-year Single-Centre Retrospective Study

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Rezumat

Tiroidectomia pentru managementul carcinomului tiroidian diferențiat și complicațiile postoperatorii precoce: un studiu retrospectiv, unicentric, pe o perioadă de 6 ani

Introducere/Obiectiv: Carcinomul tiroidian (TC) reprezintă 1% din totalitatea carcinoamele, cu o incidență mai mare la femei. Deși există controverse cu privire la selecția celui mai bun tratament chirurgical pentru TC diferențiat, tiroidectomia totală (TT) și tiroidectomia subtotală (TST) sunt încă cele două proceduri chirurgicale principale. Scopul acestui studiu a fost de a evalua rata complicațiilor precoce posttiroidectomie la pacienții supuși unei intervenții chirurgicale tiroidiene la un spital terțiar din Grecia.

Metode: Au fost incluși retrospectiv un total de 306 pacienți cu TC diferențiat la care s-a practicat o intervenție chirurgicală tiroidiană. Pacienții au fost împărțiți în două grupuri. Grupul A a inclus 214 pacienți la care s-a efectuat TT, în timp ce în grupul B (92 de pacienți) s-a practicat TST. Au fost urmărite datele demografice ale pacienților, durata intervenției și complicațiile precoce (hipoparatiroidism, hematom, infecție, paralizie temporară a nervului laringeu recurent).

Rezultate: Nu a existat nicio diferență semnificativă în ceea ce privește sexul, vârsta și durata medie a intervenției chirurgicale între cele două grupuri (P=0,47, P=0,55 și, respectiv, P=0,09). Hematomul sau infecția plăgii au fost înregistrate la 3 (1,4%) și 4

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(1,87%) dintre pacienții din grupul A, comparativ cu 2 (2,17%) și 3 (3,26%) dintre pacienții din grupul B ($P=0,63$ și $P=0,46$, respectiv). În plus, hipoparatiroidismul sau paralizia temporară a nervului laringeu recurent au fost observate la 34 (15,89%) și 13 (6,07%) dintre pacienții din grupul TT, comparativ cu 11 (11,96%) sau 9 (9,78%) dintre pacienții din grupul TST ($P=0,37$ și, respectiv, $P=0,25$).

Concluzii: Acest studiu demonstrează că tiroidectomia totală poate fi efectuată în siguranță la pacienții cu carcinom tiroidian diferențiat, fără a crește riscul de complicații precoce.

Cuvinte cheie: carcinom tiroidian diferențiat, complicații postoperatorii precoce, tiroidectomie totală, tiroidectomie subtotală, hipocalcemie

Abstract

Introduction/Objective: Thyroid carcinoma (TC) accounts for one percent of all carcinomas, with a higher incidence in women. Although there is controversy on the selection of the best surgical treatment for differentiated TC, total thyroidectomy (TT) and subtotal thyroidectomy (STT) are still the two main surgical procedures. The aim of the present study was to evaluate the early complication rates of thyroidectomy in patients undergoing thyroid surgery at a tertiary hospital in Greece.

Methods: A total of 306 patients with differentiated TC who underwent thyroid surgery were enrolled retrospectively. Patients were divided into two groups. Group A included 214 patients undergoing TT, whereas 92 patients (group B) underwent STT. Demographic details of patients, operating time, and early complications (hypoparathyroidism, hematoma, infection, temporary recurrent laryngeal nerve palsy) were noted.

Results: There was no significant difference in the sex, age, and mean operating time between the two groups ($P=0.47$, $P=0.55$, and $P=0.09$, respectively). Either hematoma or wound infection occurred in 3 (1.4%) or 4 (1.87%) of the patients undergoing TT compared to two (2.17%) or three (3.26%) of the patients undergoing STT ($P=0.63$ and $P=0.46$, respectively). In addition, either hypoparathyroidism or temporary recurrent laryngeal nerve palsy was observed in 34 (15.89%) or 13 (6.07%) of the patients undergoing TT compared with eleven (11.96%) or nine (9.78%) of the patients undergoing STT ($P=0.37$ and $P=0.25$, respectively).

Conclusions: The current study demonstrates that total thyroidectomy can be safely performed in patients with differentiated thyroid carcinoma without increasing the risk of early complications.

Key words: differentiated thyroid carcinoma, early postoperative complications, total thyroidectomy, subtotal thyroidectomy, hypocalcemia

Introduction

Thyroid disorders are one of the most common endocrine diseases. A thyroid surgery may be necessary in order that these disorders be treated. Thyroidectomy is recommended for benign as well as for the treatment of malignant disease of the thyroid gland. Thyroidectomy has potential complications. The major postoperative complications

are hypocalcemia, wound infection, hematoma and recurrent laryngeal nerve injury (1). Thyroid carcinoma (TC) accounts for one percent of all carcinomas, with a higher incidence in women. Surgery remains the preferred option for the treatment of differentiated TC and prolongs the survival of patients. Although there is controversy on the selection of the best surgical treatment for differentiated TC, total thyroidectomy (TT)

and subtotal thyroidectomy (STT) are still the two main surgical procedures (2). This clinical study was designed to evaluate the early complication rates of thyroidectomy in patients undergoing thyroid surgery at a tertiary hospital in Greece. Studies comparing the early complication rates in patients undergoing thyroidectomy and subtotal thyroidectomy have not been published so far.

Material and Methods

This retrospective trial was conducted in our institution. All patients were informed in detail of the procedure, follow-up, advantages, and complications. Ethical approval was obtained from the medical research ethics committee. Due to the retrospective nature of this study, informed consent from the Institutional Review Board of the Holy Mary the Help General University Hospital of Patras was not required. We confirmed that all methods were performed in accordance with the approved guidelines and regulations. The data were collected from the hospital registry and patient files (3). Between January 2015 and December 2020, 306 patients undergoing elective total or subtotal thyroidectomy were enrolled in the study. Inclusion criteria were age between 35 and 70 years, American Society of Anesthesiologists physical status classification I or II, and diagnosis of differentiated thyroid carcinoma (DTC) that was scheduled to be treated by elective total or subtotal thyroidectomy. Patients were divided into two groups. Group A included 214 patients undergoing TT, whereas 92 patients (group B) underwent STT.

As the name implies, total thyroidectomy cases were defined as those where complete removal of thyroid tissue was elected. In contrast, we defined subtotal thyroidectomy as the removal of most of the thyroid gland, leaving behind a small portion of approximately 2 grams of thyroid tissue, usually from the posterior thyroid gland, in order to ensure the preservation of the recurrent laryngeal nerve. Near-total thyroidectomy is typically defined as

the procedure with less than 1 ml of thyroid tissue remaining. In our institution, and as per current international guidelines, patients underwent subtotal thyroidectomy for tumors less than 1cm in the maximal diameter, or for tumors between 1 and 4 cm on highly select cases, with limited disease, no evidence of extranodal or lymph node involvement, and amenable to close follow-up with imaging.

One of the most important aspects of thyroidectomy is the selective sparing of the parathyroid glands, a pivotal step to avoid postoperative hypocalcemia. Within our institution, we aim for parathyroid preservation in every case. According to the latest publications on postoperative hypoparathyroidism, this is to be expected when accidental removal of one or more parathyroid gland occurs, yet whenever even a single parathyroid gland is preserved, spontaneous resolution is to be expected (2,3). Identification of parathyroid glands is done intraoperatively, as is the standard in many institutions. We opted for the administration of Tc-99m and intraoperative mapping in few, select cases that had indications for concomitant parathyroidectomy, and as such were excluded from the present study.

Demographic details of patients, operating time, and early complications (hypoparathyroidism, hematoma, infection, temporary recurrent laryngeal nerve palsy) were noted. Statistical analyses were done using SPSS for Windows 10. Student's t-test for normally distributed variables, U Mann-Whitney test for skewed variables, χ^2 test, and Fisher's exact tests were used to compare results between groups. A p-value < 0.05 was considered statistically significant.

Results

There was no significant difference in the sex, age and mean operating time (*Table 1*) between the two groups (P=0.47, P=0.55 and P=0.09, respectively). Either hematoma or wound infection occurred in 3 (1.4%) or 4 (1.87%) of the patients undergoing TT compared with two (2.17%) or three (3.26%) of the patients undergoing STT (P=0.63 and P=0.46, respectively. In

Table 1. Baseline characteristics of the study population and early postoperative complications in patients undergoing total thyroidectomy (TT) and subtotal thyroidectomy (STT) for differentiated thyroid carcinoma

Variable	Group A Total thyroidectomy	Group B Subtotal thyroidectomy	P value
Number of patients (n=306).	214	92	
Males/Females (68/238).	50/164	18/74	>0.05
Age (Mean \pm SD) (years).	54.1 \pm 4.9	54.4 \pm 3.5	>0.05
Operative time (Mean \pm SD) (minutes).	79.8 \pm 14.1	81.9 \pm 7.4	>0.05
Hematoma	3	2	>0.05
Wound infection	4	3	>0.05
Hypoparathyroidism	34	11	>0.05
Temporary recurrent laryngeal nerve palsy	13	9	>0.05

addition, either hypoparathyroidism or temporary recurrent laryngeal nerve palsy (TRLNP) was observed in 34 (15.89%) or 13 (6.07%) of the patients undergoing TT compared with eleven (11.96%) or nine (9.78%) of the patients undergoing STT (P=0.37 and P=0.25, respectively).

Bivariate and multivariate analysis did not reveal any underlying differences between patients in terms of age or BMI that experienced each of the complications and those that did not between the two groups.

Discussion

Total thyroidectomy is preferred mainly in patients with nodules that are suspicious cytologically or sonographically for malignancy, are > 4 cm and are found with positive mutations specific for carcinoma (for instance, TERT promoter mutations). It could be also considered in patients with indeterminate nodules with bilateral nodular disease and want to avoid a completion thyroidectomy if the indeterminate nodule is malignant, significant comorbidities and a history of childhood neck radiation or familial thyroid cancer, because the risk of cancer in the remaining thyroid tissue is higher. It is also proposed as the initial surgery when there is a high risk of aggressive disease and local recurrence, such as when nodules have radiologic evidence of extrathyroidal extension (ETE) or the adjacent structures are invaded. Shrime et al. concluded that initial total thyroidectomy is a more cost-effective option than initial hemithyroidectomy. Total thyroidectomy can

be accompanied by lymph node (LN) dissection of the affected compartments in case of metastatic LNs (4-5). Subtotal thyroidectomy is the procedure in which a remnant of the thyroid is left at the tracheal attachments while the rest of the gland is removed. This procedure is performed for multinodular goiter and some cases of thyrotoxicosis. Proposed indications for initial less-than-total thyroidectomy (LTT) based on tumor type and size are papillary thyroid carcinoma (PTC) \leq 1 cm in adults (unifocal and non-metastatic), minimally invasive follicular thyroid carcinoma (FTC), differentiated thyroid carcinoma (DTC) in children, sporadic medullary microcarcinoma, undifferentiated thyroid carcinoma (UTC), no unusual histopathological variants such as tall cell, columnar cell, solid, diffuse sclerosing, trabecular, or Hürthle cell (6).

The three main complications that can occur in all types of thyroid surgery are bleeding, recurrent laryngeal nerve (RLN) palsy and postoperative hypocalcemia. Other complications include formation of seroma, dysphagia, superior laryngeal nerve (SLN) injury, hypertrophic scarring, recurrence, esophageal or tracheal wounds, infections, thyrotoxic storm, tracheomalacia, pneumothorax or pneumomediastinum and rare complications by hyperextension of the neck (7-10).

Postoperative Hemorrhage

The thyroid gland has very rich blood supply resulting in increased possibility of bleeding and hematoma formation. Factors that could

cause bleeding are poor coagulation, failure of clamp and tie technique, postoperative increased blood pressure and remnant thyroid tissue damage (11). This usually occurs the first 6-12 hours after thyroidectomy and careful monitoring is required (7,10). Risk factors for postoperative bleeding include male sex, cases of toxic goiter and total thyroidectomy, but can occur after any type of thyroid surgery (12). Clinical presentation of bleeding consists of neck swelling, skin ecchymosis, neck pain and in case of airway obstruction severe manifestations such as stridor, hypoxia, dyspnea (8). Nicholson et al. reported that the cases of hematoma requiring reoperation were similar for total thyroidectomy, hemithyroidectomy and completion thyroidectomy (13). Hauch et al. stated that unilateral thyroidectomy has lower rates of bleeding and hematoma than total thyroidectomy (14). Sawant et al stated that after completion thyroidectomy, 3% of patients suffered from postoperative hematoma (15). In their review, Padur et al mentioned that the incidence of postoperative hematoma was not different between total and subtotal thyroidectomy (16). Nixon et al reported that in 19 patients who underwent isthmusectomy, one was found with wound hematoma (17). Christou and Mathonnet stated that the risk of postoperative hematoma was 0-6.5% after total thyroidectomy (10). Leyre et al found that 70 compressive hematomas in a sample of 6744 patients, 10% of these were observed 24h after the total thyroidectomy (18). Pandey et al mentioned that hematoma formation after thyroid surgery was a rare complication which occurred in less than 1 to 2% (9). In their review, Padur et al noted that the incidence of postoperative hematoma was not different between total and subtotal thyroidectomy (16).

Recurrent Laryngeal Nerve Damage

The recurrent laryngeal nerve is a branch of the vagus nerve that is responsible for the movement of all laryngeal muscles except the cricothyroid muscles. RLN damage often occurs near the entrance of the larynx.

Clinical manifestations of unilateral paralysis include severe dysphonia, paralytic aphonia and episodes of pulmonary aspiration. In bilateral paralysis the symptoms are more severe and consist of acute stridor, respiratory distress and aphonia requiring emergency intubation or tracheostomy. Regarding the severity of the injury, symptoms can be temporary or permanent (8). Prevention of RLN damage includes preoperative laryngoscopy, meticulous operative technique, and neural monitoring (10). Nicholson et al reported that the cases of temporary vocal cord paralysis were similar for total thyroidectomy, hemithyroidectomy, and completion thyroidectomy (13). Hauch et al stated that hemithyroidectomy has lower rates of vocal cord paralysis than total thyroidectomy (14). Sawant et al stated that after completion thyroidectomy, 2% of patients suffered from permanent RLN palsy (15). In their review, Padur et al mentioned that the incidence of RLN palsy was not different between total and subtotal thyroidectomy (16). Gough and Wilkinson reported that RLN paralysis is one of the most common complications of total thyroidectomy which accounts for 0.7% of cases (19). Skilbeck et al found out that isthmusectomy minimizes the danger of potential damage to recurrent laryngeal nerve. Nixon et al reached the same conclusion (17,20). Christou and Mathonnet, after reviewing the current literature, found that risk factors for RLN damage consist of the presence of Grave's disease, chronic thyroiditis and increased goiter volume which causes the nerve to be stressed thus exposing it to a greater risk of injury (10). In their review, Ozbas et al mentioned the results of previous studies which suggested that the risk of permanent RLN paralysis was estimated 0-0.7% after total thyroidectomy and 0-1.3% after bilateral subtotal thyroidectomy (21).

Postoperative Hypocalcemia

Hypocalcemia after thyroid surgery is almost always caused by hypoparathyroidism. Central neck dissection, reoperations, increased goiter

size and thyroid inflammations like Graves' disease and thyroiditis. Clinical presentation of hypocalcemia includes tingling, tetany, Trousseau and Chvostek signs, laryngospasm and occasionally psychosis and hallucinations (7). Hauch et al stated that hypoparathyroidism was the most common complication and hemithyroidectomy has lower rates of hypoparathyroidism than total thyroidectomy (14). On the contrary, Nicholson et al reported that the cases of temporary hypoparathyroidism were similar for total thyroidectomy, hemithyroidectomy, and completion thyroidectomy (13). Gough in 1992 mentioned a 1970s study where the rate of hypoparathyroidism was five times higher in total than subtotal thyroidectomy (19).

Based on the results of our research there is no significant difference in occurrences of hematoma, wound infection, hypoparathyroidism and temporary RLN palsy between the two groups. Of our patients, 1.4% who underwent total thyroidectomy suffered from postoperative hematoma, which lies within the range of current literature (0-6.5%)(10). In our study the incidence of postoperative hematoma was not statistically significant (1.4% TT – 2.17% STT) between the two procedures, which agrees with the current retrospective studies (0-6.5% TT) (22). There was no available data for wound infection rates in the current literature between the two methods. The rates of hypoparathyroidism in our study were 15.89% after TT and 11.96% after STT, which is not in accordance with previous prospective studies, possibly because of different surgeon volume, surgical techniques, and equipment. In temporary RLN palsy the rate difference is not statistically significant, which is in line with data of current literature. However, the individual percentages in total and subtotal were higher in our institution (15.89% TT - 11.96% STT) compared to the current literature (0-0.7% TT vs 0-1.3% STT), possibly due to different surgeon volume, surgical techniques, and equipment (22).

Surgical Site Infection

Surgical Site Infection (SSI) rates in both patient cohorts were minimal and did not indicate any trend for statistical significance (1.87% for TT group versus 3.2% in the STT group, $p>0.05$) There is quite a variability in reported SSI rates after thyroidectomy in literature. Reports range from less than 1%, up to 2.6% of the patients involved (24-32). Authors have successfully identified operative time and obesity as predictive factors for SSI incurrence in thyroidectomy procedures (25, 26). Our reported rates seem to be in line with those reported in the literature, although large patient cohorts, incorporating patients from multiple centers seem to indicate that the true reported percentage of SSI might be even lower. Between the patients that exhibited SSI, there was no statistically significant difference in BMI or age, and the sample itself (4 and 3 patients respectively) is too small to draw any conclusions at any rate. The variability behind the reported SSI rates, indicates that this complication could be dependent upon institutional rather than patient factors, such as surgeon technique, antiseptic protocols and postoperative anti-biotic administration. Age, lymph node dissection and presence of postoperative drains were also identified in a nested case-control study with lymph node dissection being reported as the strongest predictor, with a reported OR of 3.22 (28). Currently, there are no reports in literature specific for comparing infection rates between TT and STT, and the associations with several confounders. This is a gap in literature that needs to be addressed with larger patient cohorts.

Conclusion

The current study demonstrates that total thyroidectomy can be safely performed in patients with differentiated thyroid carcinoma without increasing risk of early complication.

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