The efficacy and safety of total thyroidectomy in the management of benign thyroid diseases

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Abstract

Background: Total thyroidectomy is currently the preferred treatment for thyroid cancer, multinodular goitre and Graves disease,· however, many surgeons choose not to perform total thyroidectomy to treat benign thyroid diseases owing to the associated risk of postoperative hypoparathyroidism and recurrent laryngeal nerve damage. We followed up 100 thyroidectomies performed for benign thyroid diseases when surgery was indicated. We sought to assess whether the results support the hypothesis that total thyroidectomy is as safe and more effective as subtotal thyroidectomy and can be considered as the optimal surgical approach for treating benign thyroid diseases.

Methods: A total of 100 patients underwent thyroidectomy between January 2008 and June 2009. We excluded patients with thyroid cancer or suspicion of thyroid malignancy. We evaluated operative time, intraoperative blood loss, cancer incidence, complication rates, local recurrence rate and long-term outcome after total and subtotal thyroidectomy.

Results: All patients were diagnosed before surgery to have benign thyroid disease by fine needle aspirate. The incidence of permanent recurrent laryngeal nerve palsy (unilateral or bilateral) was 0% in both groups, whereas the incidence of temporary unilateral recurrent laryngeal nerve palsy was 4% in cases of total thyroidectomy and 2% in cases of subtotal thyroidectomy. Permanent hypocalcemia occurred in 2% in each group and overall temporary hypocalcemia occurred in 10% ofpatients with total thyroidectomy and 8% ofpatients with subtotal thyroidectomy. Hemorrhage requiring repeat surgery occurred in 2% of patients with total thyroidectomy and 4% of patients with subtotal thyroidectomy. There was no wound infection, and postoperative mortality was 0%. Incidental finding of cancer appeared in 8% of patients with total thyroidectomy and 18% of patients with subtotal thyroidectomy. We observed no disease recurrence during a follow-up of 18 months in patients with total thyroidectomy, while a high rate of recurrence (8%) appeared in patients with subtotal thyroidectomy in the same follow-up period.

Conclusion: Total thyroidectomy is safe and is associated with a low incidence of disabilities. Complication rates for recurrent laryngeal nerve palsy and hypoparathyroidism are approximately similar to results of those with subtotal thyroidectomy. Furthermore, total thyroidectomy seems to be the optimal procedure, when surgery is indicated, for benign thyroid diseases as it has the advantages of immediate and permanent cure and no recurrences and higher rate of detection of occult cancer.

Introduction:

Historically, the risks associated with major surgery for treating thyroid diseases and the problems of adequate hormonal replacement have deterred surgeons from performing total thyroidectomies. In fact, thyroid surgery was rarely performed until the late 19th century; total thyroidectomies were only performed occasionally for indications other than cancer until the last quarter of the twentieth century.[1] The use of total thyroidectomy remains controversial for small differentiated thyroid carcinomas, but even more controversial is its use to treat benign diseases.[2] Most surgeons

avoid the procedure owing to the possible complications such as permanent recurrent laryngeal nerve palsy and permanent hypoparathyroidism; subtotal thyroidectomy has been the preferred operation for benign thyroid diseases.2 Although the extent of resection for benign diseases remains controversial, an increasing number of total thyroidectomies are currently performed in specialist endocrine surgery units, and the indications for this procedure include Graves disease and multinodular goitre.

Many surgeons still hesitate from doing total thyroidectomy in benign thyroid diseases in order not to increase the rate of complications associated with surgery such as risk of postoperative hypoparathyroidism (up to 12.5%) and recurrent laryngeal nerve palsy (up to 2.3%).3 However, some studies showed that the complication rates of permanent recurrent laryngeal nerve palsy (0--1.3%) and permanent hypoparathyroidism (1%) following subtotal thyroidectomy are similar to those following total thyroidectomy.4-9 In addition, the disadvantages of subtotal thyroidectomy to treat Graves disease are that the procedure does not prevent persistent or recurrent disease in up to 20% of patients; it does not stop the process of the disease and, as a result, it cannot stop the progress of ophthalmopathy; and it does not address hypothyroidism in up to 70% of patients.

The disadvantages of subtotal thyroidectomy to treat multinodular goitre are that the procedure does not reduce the risk of persisting symptoms and has a high recurrence rate (30o/o-50%) owing to gland remnants, even under suppression hormonal treatment with L-thyroxine2. Disease recurrence usually requires a repeat surgery, which greatly increases the risk (up to 20 times) of damage to parathyroid glands and laryngeal nerves.lO In contrast, total thyroidectomy eliminates all abnormal tissue in the neck and lowers recurrence rates for Graves disease and multinodular goitre. Furthermore, after total thyroidectomy, hormone replacement with L-thyroxine is relatively easy and can be achieved by monitoring the thyroid hormone serum levels.

In our institute, surgeons always do total thyroidectomy for thyroid cancer and total or subtotal thyroidectomy for benign diseases and for recurrent disease after previous thyroid surgery.

We sought to assess whether total thyroidectomy is a safe procedure with low complication rates of permanent recurrent laryngeal nerve palsy and permanent hypoparathyroidism. We also sought to evaluate the long-term outcomes including the management of hypothyroidism and the recurrence rates for benign disease and to compare the results with those of subtotal thyroidectomy in terms of efficacy and safety.

Methods:

Between January 2008 and June 2009, a prospective randomized (by closed envelope method) study of 100 patients who presented with benign thyroid diseases undergoing thyroid surgery was conducted at Head and Neck Surgery unit, Faculty of Medicine, Alexandria University and Makassed General Hospital. Patients were randomly assigned to one of two groups by closed envelope method: total thyroidectomy or subtotal thyroidectomy.

All patients were selected on the basis of the following criteria: evidence of thyroid diseases by preoperative ultrasound examination, absence of family history of malignant thyroid disease, absence of history of previous neck surgery or irradiation.

All patients provided informed consent after a thorough explanation of the surgical procedure by the surgeon. Each patient filled a history sheet that included the main data and symptoms of his disease.

Inclusion criteria:

All patients with benign thyroid diseases (by FNAC), when surgery is indicated.

Exclusion criteria:

Patients with documented malignant thyroid disease.

Patients showing suspicious findings of malignant disease during surgery.

Patients with previous parathyroid disease.

Patients with family history of thyroid cancer.

Patients with previous neck surgery or neck irradiation.

Preoperative assessment:

Patient's data were collected including age, sex, past history, and family history. Routine laboratory workup was done for all of them including complete blood count, coagulation profile, fasting blood sugar, and blood urea.

All patients had measurements of serum thyrotropin, thyroxine, triiodothyroxine, thyroid antibodies and calcium, and ultrasound estimation of thyroid volume and morphology. Where appropriate (e.g., large or retrostemal goitres), we obtained a computed tomography scan of the neck. All thyrotoxic patients were rendered euthyroid before surgery to prevent perioperative thyroid crisis.

Procedures:

Group I with total thyroidectomy: Formal total thyroidectomy was done with dissection of the thyroid gland after identifying and preserving both recurrent laryngeal nerves and 3-4 parathyroid glands and keeping them in place with their vasculature. The strap muscles were then approximated and the neck closed.

Group II with subtotal thyroidectomy: dissection was done in the same way as total thyroidectomy, once the superior pole vessels were divided and the thyroid lobe mobilized anteriorly, the thyroid lobe was cross-clamped with a Mayo clamp, leaving approximately 4 g of the posterior portion of the thyroid. The thyroid remnant was suture ligated, taking care to avoid injury to the recurrent laryngeal nerve. In both groups, patients were discharged within 3-4 days after surgery.

Intraoperative assessment:

The data concerning the following parameters were collected: type of operation, operative time, intraoperative bleeding and estimated blood loss, and intraoperative evidence of malignancy.

Postoperative management:

Postoperative follow-up included indirect laryngoscope to check vocal cord mobility and measurement of serum calcium 24 hours and 48 hours postoperatively, hypocalcaemia was defined as serum calcium less than 8.0 mg/ dl.

Patients were all assessed for postoperative wound complications including hematoma or wound infection.

The entire resected surgical specimens were pathologically examined with comment on the final pathological diagnosis.

Data for all patients were then collected concerning final pathological diagnosis, hospital stay, and complication rate.

Patients were further followed-up by the means of careful neck examination by palpation, calcium level in blood after six months and neck ultrasonography at 12 months postoperatively.

In patients who were asymptomatic and did not require calcium supplementation, we defined temporary hypocalcemia as a calcium level lower than 8.0 mg/dL in at least 2 consecutive samples (daily for 2 consecutive days). In these patients, hypocalcemia resolved within days. Conversely, in patients who were symptomatic and required calcium supplementation, we considered temporary hypocalcemia to be severe when calcium levels remained lower than 8.0 mg/dL for more than 3 days. In these patients, hypocalcemia resolved within 6 months. In patients who required vitamin D and calcium supplementation for more than 6 months, we considered hypoparathyroidism to be permanent.

We defined recurrent laryngeal nerve palsy as hoarseness associated with vocal cord paralysis at laryngoscopy within 6 months postoperatively. After 6 months, we considered recurrent laryngeal nerve palsy to be permanent At the time of extubation, the anesthesiologist evaluated vocal cord motility in all patients. Hormonal treatment with L-thyroxine began within 5 days after thyroidectomy in all patients.

The data of the two groups, total thyroidectomy (n =50), and subtotal thyroidectomy (n =50) were analyzed and compared for their statistical significance with a P value less than 0.05 was considered statistically significant.

Follow-up:

The surgeons conducted the follow-up visits for all patients. At 1, 6 and 12 months postoperatively. The surgeons evaluated patients' hormonal replacement, vocal cord motility, parathyroid function and therapeutic outcome. Evaluation included clinical examination, serum thyroid hormones and calcium measurements. In patients with

recurrent laryngeal nerve palsy an otolaryngologist performed a laryngoscopy at 1, 6 and 12 months postoperatively to monitor vocal cord function.

Results:

Between January 2008 and June 2009, 100 patients with benign thyroid disease presented to the surgery department and undetwent either total (50 patients) or subtotal thyroidectomy (50 patients). Of these, 15 were men and 85 were women. The first group with total thyroidectomy included 9 men and 41 women, while the second group with subtotal thyroidectomy included 6 women and 44 men. The median age of patients was 42.54 (range 17--69) years in the first group and 41.16 (range 20-56) in the second group. None of the patients had previous exposure of his or her neck to radiation, which increases the risk of thyroid carcinoma. All patients were diagnosed before surgery to have benign thyroid disease by ultrasound and fme needle aspirate cytology, where the first group included 9 patients presenting with single thyroid nodule and 41 patients with multinodular goiter; whereas the second group included 12 patients with single thyroid nodule and 38 patients with multinodular goiter.

All the patients included in the present study were examined by indirect laryngoscopy for vocal folds mobility prior to surgery and all of them showed normal vocal fold mobility. All patients had normal thyroid laboratory function tests and normal levels of serum calcium (8.5-10.4 mg/dl) prior to surgery.

The mean operative time for the first group with total thyroidectomy was (120.1± 29.23 min), while for the second group with subtotal thyroidectomy, the mean operative time was (119.9± 27.03 min).

The amount of intraoperative blood loss was estimated for all operative procedures performed. The mean intraoperative blood loss for cases of total thyroidectomy was (59.80±29.76 ml), while for cases of subtotal thyroidectomy the mean intraoperative blood loss was (71.50±31.56 ml).

Postoperative bleeding and hematoma formation requiring surgical intervention occurred in 1 patient (2%) with total thyroidectomy and in 2 patients (4%) with subtotal thyroidectomy.

Among all patients, there was no permanent recurrent laryngeal nerve palsy, although, three cases of unilateral temporary palsy occurred and they were divided as two cases with total thyroidectomy (4%) and one case with subtotal thyroidectomy (2%). Complete recovery was the rule for all the three patients and they regained their normal voice quality.

Transient hypocalcemia occurred in five patients (10%) with total thyroidectomy and four patients (8%) with subtotal thyroidectomy. Permanent hypocalcemia (>6months) occurred in 1 patient (2%) in each group.

All thyroid specimens were subjected for histo-pathologic examination. Results showed benign disease in 41 patients in group I and 46 patients in group II. Among these results, multinodular goiter (78%) was the most common; followed by Grave's disease (11%), adenoma (8%) and thyroiditis (3%).

Incidental thyroid cancer was detected in nine (18%) patients in group I and four (8%) patients in group II, thus requiring completion thyroidectomy and indicating the possibility of many cases of undiagnosed cancer in the second group. Of these 13 cases, incidental papillary carcinoma appeared in 11 cases while medullary carcinoma appeared in 2 patients.

Thyroid pathology	Group I (Total thyroidectomy)	Group II (Subtotal thyroidectomy)
Benign thyroid diseases	41 (82%)	46 (92%)
Incidental cancer	9 (18%)	4 (8%)

We observed no disease recurrence during a follow-up of 18 months in patients with total thyroidectomy, while a high rate of recurrence (n=4, 8%) appeared in patients with subtotal thyroidectomy in the same follow-up period.

None of the patients with total thyroidectomy required a second completion operation, while 8 patients (16%) with subtotal thyroidectomy required a completion surgery (4 patients because of incidental cancer and 4 patients because of recurrence).

There was no wound infection and no mortality in both groups.

Data of both groups, total thyroidectomy (n =50), and subtotal thyroidectomy (n =50) were analyzed andcompared for their statistical significance with a P value less than 0.05 was considered statistically significant.

Complication	Total thyroidectomy, No.(%) of patients	Subtotal thyroidectomy, No.(%) of patients	P value
Permanent hypocalcemia	1 (2%)	1 (2%)	0.74
Transient hypocalcemia	5 (10%)	4 (8%)	0.48
Permanent recurrent laryngeal nerve palsy	0	0	—
Transient unilateral recurrent laryngeal nerve palsy	2(4%)	1 (2%)	0.5
Hemorrhage	1(2%)	2(4%)	0.5
Wound infection	0	0	—
Incidental detection of cancer	9 (18%)	4 (8%)	0.017*
Recurrence	0	4 (8%)	0.04*
Need for completion thyroidectomy	0	8 (16%)	0.003*
Mortality	0	0	—

Denotes statistically significant values.

Discussion:

Benign thyroid diseases are very common nowadays. The most common benign thyroid diseases are multinodular goiter (78.8%), Graves disease (17.8%) and recurrent (after previous partial thyroidectomy) nodular goiter (3.4%).11

Benign multinodular goiter is one of the most common endocrine surgical problems; the appropriate surgical procedure for its effective and safe management is a matter of debate.I2 Although total thyroidectomy is the procedure of choice in patients with thyroid carcinoma, this surgical approach has emerged as a surgical option to treat patients with benign multinodular goiter (BMNG), especially in endemically iodine-deficient regions.13 Many surgeons still hesitate from doing total thyroidectomy in benign thyroid diseases in order not to increase the rate of complications associated with surgery such as risk of postoperative hypoparathyroidism (up to 12.5%) and recurrent laryngeal nerve palsy {up to 2.3%).14

There is increasing recognition that total thyroidectomy is also the appropriate surgical treatment for benign toxic and nontoxic multinodular goitre, particularly when the

nodular disease involves both lobes),4,10,15-17 The advantages of total thyroidectomy in such cases are the prompt relief of symptoms; provision of a defmite histological diagnosis, especially when the clinical features indicate the possibility of thyroid malignancy (the reported risk is about 5%-10%); and no risk of disease recurrence. On the other hand, nontotal thyroidectomy, such as subtotal thyroidectomy or unilateral lobectomy, is a less satisfactory procedure because, by leaving residual thyroid tissue, the patient is exposed to a higher risk of recurrent disease (23o/o-45%) that is not treatable by thyroxine suppression therapy and will, therefore, involve repeat surgery.1,2,18 Moreover, nontotal thyroidectomy does not avoid the risk of postoperative complications. In fact, the complication risk of nontotal thyroidectomy is similar to that of total thyroidectomy, and the risk of repeat surgery owing to recurrence is up to 20 times greater with nontotal thyroidectomy,lO

The aim of this study is to compare the outcome of both techniques of total thyroidectomy and subtotal thyroidectomy in relation to efficacy, safety and possible complications. The groups of patients included in this study were well matched in the terms of age, gender, preoperative laboratory test results and surgical indications, therefore a comparison seemed possible.

Preoperative estimation of thyroid disease by ultrasound neck examination, thyroid function tests and fine needle aspiration cytology were considered to be the corner stone for selection of patients eligible to be included in the study. In this series, the main inclusion characteristic was a benign thyroid disease as documented by ultrasound and FNAC.

There was no statistical difference between both groups concerning preoperative data including age, sex, preoperative presentation, laboratory investigations and FNAC results.

Operative time and intraoperative blood loss were estimated in both groups and showed no statistical difference (p=0.972 and p=0.59 respectively).

The main complications of thyroid surgery are associated with injury of parathyroid glands with subsequent hypocalcemia and recurrent

laryngeal nerves. The risk of recurrence or incidental finding of cancer requiring completion thyroidectomy and a second operation with its subsequent hazards is extremely important.

In a certain study, it was proved that a grade C recommendation can be made about total thyroidectomy being a safe and effective procedure for benign multinodular goiters in the hands of expert surgeons, based on the extensive level N evidence, and limited level II and level ill evidence, which show that the risk of permanent vocal cord palsy and hypoparathyroidism associated with total thyroidectomy is below the acceptable 2% rate, but not without exceptions.12

Hypocalcaemia caused by transient or definitive hypoparathyroidism is the most frequent complication after thyroidectomyl9.

A report from Eleni I. Efremidou et al showed that the rate of temporary hypocalcemia was 7.3% while permanent hypocalcemia occurred in 0.3% of patients after total thyroidectomy)! Gough and Wilkinson! reported permanent hypoparathyroidism following total thyroidectomy at the rate of 2.2%. In our study, temporary hypocalcemia occurred in 10% in patients with total thyroidectomy and 8% in patients with subtotal thyroidectomy; while permanent hypocalcemia occurred in 2% in each group.

The above data show that the present results are comparable with other studies and that transient and permanent hypocalcemia following total thyroidectomy occurs in acceptable rates when compared to subtotal thyroidectomy, with statistically insignificant values (p=0.487).

Aytac Bet al,2o reported that following total thyroidectomy, unilateral vocal cord problems occurred in 3.8% of cases and in 1.2% of cases it became permanent.

The present study showed transient unilateral recurrent laryngeal nerve palsy in 1 patient (2%) following subtotal thyroidectomy and in 2 patients (4%) following total thyroidectomy and all these patients improved within three months resulting in 0% of cases having permanent recurrent laryngeal nerve disease. The important issue in the present results was that there was no statistical

significance between nerve injury following total and subtotal procedures (p=0.5).

Eleni I Efremidou et alll reported postoperative hemorrhage requiring surgical hemostasis in 0.2% of patients, no wound infection and no mortality. The present study showed that postoperative hemorrhage occurred in 2% and 4% of total and subtotal procedures respectively with no statistical significance between both groups (p=0.5). There was no wound infection and no mortality.

Despite the recent wide availability of ultrasonography and fine-needle aspiration biopsy, endocrine surgeons often encounter incidental papillary carcinoma (IPC) that is a papillary carcinoma that had gone undetected by preoperative imaging studies but was identified by pathological examination of surgical specimens resected for benign thyroid diseases.[21]

Incidental thyroid cancers are detected in 3%-16.6% of apparently benign goiters in numerous studies, mostly providing level IV evidence, one third of which would need further surgical treatment after subtotal thyroidectomy.[12]

In the present study, incidental thyroid cancers were detected in 4 patients (8%) after subtotal thyroidectomy and in 9 patients (18%) after total thyroidectomy. These patients with subtotal thyroidectomy needed a completion thyroidectomy for their malignant disease with more complications. In addition, the high number of incidental cancers detected after total thyroidectomy show that there are some cases with thyroid cancer left undiagnosed after subtotal thyroidectomy. Statistical analysis showed significant difference between both groups concerning detection of incidental thyroid cancer (p=0.017).

Another advantage of total thyroidectomy is the prompt relief of symptoms and no risk of disease recurrence. On the other hand, subtotal thyroidectomy is a less satisfactory procedure because, by leaving residual thyroid tissue, the patient is exposed to a higher risk of recurrent disease (23o/o-45%) that is not treatable by thyroxine suppression therapy and will, therefore, involve repeat surgery.[11] Moreover, subtotal thyroidectomy does not avoid the risk of postoperative complications.

In fact, the complication risk of subtotal thyroidectomy is similar to that of total thyroidectomy, and the risk of repeat surgery owing to recurrence is up to 20 times greater with subtotal thyroidectomy.[to]

In this study, and by ultrasound examination after 18 months of surgery, there was no evidence of recurrence after total thyroidectomy while four patients (8%) showed a recurrent disease after subtotal thyroidectomy; thus requiring a repeat surgery to complete thyroidectomy, with a significant statistical difference (p=0.049).

Completion thyroidectomy due to incidental finding of cancer or for recurrence of disease was needed in 8 patients (16%) after subtotal thyroidectomy, while none of the patients who had total thyroidectomy needed that. This showed a great statistical difference (p=0.003).

Conclusion:

Total thyroidectomy can be safely done with a low complication rate. Data from many studies show no significant difference in the rate of postoperative complications (e.g., recurrent laryngeal nerve injury, hypoparathyroidism, hemorrhage) associated with total thyroidectomy compared with subtotal thyroidectomy.

As a result, total thyroidectomy is now widely accepted for the management of both malignant and benign thyroid diseases. Our data support that total thyroidectomy is a valuable option, when surgery is indicated, for treating benign thyroid conditions such as multinodular goitre.

It has been shown that total thyroidectomy achieves immediate and permanent cure with no risk of disease recurrence or repeat surgeries.

Our data also suggest that there is an increased risk for malignancy among patients with benign thyroid conditions, which is detected more frequently when total thyroidectomy is performed. In such patients total thyroidectomy offers a definite management of thyroid cancer.

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