The efficacy and safety of total thyroidectomy in the management of benign thyroid disease: a review of 932 cases

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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 reviewed 932 total thyroidectomies performed for benign thyroid diseases when surgery was indicated. We sought to assess whether the results support the hypothesis that total thyroidectomy is safe and can be considered as the optimal surgical approach for treating benign thyroid diseases.

Methods: A total of 932 patients underwent thyroidectomy between 1985 and 2005. We excluded patients with thyroid cancer or suspicion of thyroid malignancy. We evaluated indications for total thyroidectomy, cancer incidence, complication rates, local recurrence rate and long-term outcome after total thyroidectomy.

Results: Diagnoses before surgery were multinodular goitre (n = 734, 78.8%), Graves disease (n = 166, 17.8%) and recurrent (after previous partial thyroidectomy) nodular goitre (n = 32, 3.4%). The incidence of permanent bilateral recurrent laryngeal nerve palsy was 0% and that of permanent unilateral recurrent laryngeal nerve palsy was 0.2%, whereas the incidence of temporary unilateral recurrent laryngeal nerve palsy was 1.3%. Permanent hypocalcemia occurred in 0.3% and overall temporary hypocalcemia occurred in 7.3% of patients. Hemorrhage requiring repeat surgery occurred in 0.2% of patients. There was no wound infection, and postoperative mortality was 0%. We observed no disease recurrences during a median follow-up of 9 (range 2–20) years.

Conclusion: Total thyroidectomy is safe and is associated with a low incidence of disabilities. Complication rates for recurrent laryngeal nerve palsy and hypoparathyroidism are similar to results of specialist endocrine surgery units. Furthermore, total thyroidectomy seems to be the optimal procedure, when surgery is indicated, for Graves disease and multinodular goitre, as total thyroidectomy has the advantages of immediate and permanent cure and no recurrences.
H
torically, 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. The use of total thyroidectomy remains controversial for small differentiated thyroid carcinomas, but even more controversial is its use to treat benign diseases. 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. 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.

Furthermore, it has been shown 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. 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 (30%–50%) owing to gland remnants, even under suppression hormonal treatment with L-thyroxine. Disease recurrence usually requires a repeat surgery, which greatly increases the risk (up to 20 times) of damage to parathyroid glands and laryngeal nerves.

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. As a result, total thyroidectomy is currently regarded as the surgical procedure of choice to treat Graves disease and multinodular goitre.

Since 1985, in the First Surgical Department in our institution, K.J.M. and his team have been performing only 2 types of thyroid surgery: total lobectomy with isthmusectomy (hemithyroidectomy) and total thyroidectomy. We perform total thyroidectomy to treat thyroid cancer and benign conditions such as Graves disease, multinodular goitre and other less common conditions (e.g., thyroiditis), in cases where surgery is indicated. We also perform total thyroidectomy for recurrent goitre after previous partial thyroidec- tomy (lobectomy/isthmusectomy, subtotal thyroidectomy).

We sought to assess whether total thyroidectomy can be carried out safely with low complication rates of permanent recurrent laryngeal nerve palsy and permanent hypoparathyroidism, similar to results reported from world-class specialist endocrine surgery units. We also sought to evaluate the long-term outcomes including the management of hypothyroidism and the recurrence rates for Graves disease and multinodular goitre.

METHODS

We conducted a retrospective review of patients who underwent total thyroidectomies between 1985 and 2005 in the First Surgical Department at University Hospital of Alexandroupolis. A specialist endocrine surgeon (K.J.M.) performed all procedures at a university tertiary teaching hospital.

We extracted data on sex, age, details of thyroid disease, preoperative assessment, recurrent laryngeal nerve palsy and hypoparathyroidism rates, rates of other postoperative complications, final pathology and recurrence rates from departments’ medical records.

We excluded patients with documented thyroid cancer or cytological suspicion of malignancy from the study. We also excluded patients with a family history of thyroid malignancy, although 29 (3.1%) had some family history of benign thyroid diseases.

Preoperative assessment

Clinical assessments in all patients included measurements of serum thyrotropin, thyroxine, triiodothyroxine, thyroid antibodies and calcium, and ultrasound estimation of
thyroid volume and morphology. In many cases, preoperative assessment included radioactive iodine imaging of the thyroid gland. Where appropriate (e.g., large or retrosternal goitres), we obtained a computed tomography scan of the neck. To exclude pre-existing vocal cord palsy, an otolaryngologist assessed vocal cord motility preoperatively in all patients.

All thyrotoxic patients received pharmacologic therapy, which was continued until the day of the surgery, to prevent perioperative thyroid crisis.

Surgical procedure

Surgical dissection of the thyroid took place after the identification and preservation of both laryngeal nerves and superior and inferior parathyroid glands. In all patients, we identified 3–4 parathyroid glands and left them in situ with their own vascularization. If we inadvertently removed or devascularized a parathyroid gland, we autotransplanted the gland into the ipsilateral sternocleidomastoid muscle. We drained the neck with bilateral suction drains for 48 hours, and patients were usually discharged within 4 days after surgery.

Postoperative management

Postoperatively, we measured serum calcium on the day of the surgery and twice daily on subsequent days in all patients.

We defined postoperative hypocalcemia as a calcium level lower than 8.0 mg/dL (reference range 8.2–10.2 mg/dL). In patients who were asymptomatic and did not require vitamin D or calcium supplementation, we defined temporary hypocalcemia as a calcium level lower than 8.0 mg/dL in at least 2 consecutive samples (twice daily for 3 days). In these patients, hypocalcemia resolved within days. Conversely, in patients who were symptomatic and required vitamin D with or without 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. Because unilateral recurrent laryngeal nerve palsy sometimes can be clinically difficult to detect, an otolaryngologist performed a laryngoscopy in all patients before they were discharged.

Hormonal treatment with L-thyroxine began within 5 days after thyroidectomy in all patients.

Follow-up

The same team of 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. Beyond 12 months, the surgeons assessed each patient once a year for 5 years to ensure accurate monitoring of possible local recurrence.

The surgeons evaluated patients with severe or permanent hypocalcemia every 3 months (at 1, 3, 6, 9 and 12 mo) postoperatively until their serum calcium normalized, with or without vitamin D and calcium supplementation.

In patients with recurrent laryngeal nerve palsy an otolaryngologist performed a laryngoscopy at 1, 6, 12 and 18 months postoperatively to monitor vocal cord function.

RESULTS

Between January 1985 and December 2005, 932 patients with benign thyroid disease underwent total thyroidectomy. Of these, 194 were men and 738 were women (ratio 1:3.8). The median age of patients was 49 (range 16–82) years. Of the 932 total thyroidectomies, 900 were single procedures and 32 were completion total thyroidectomies in patients with recurrent goitres after previous thyroid surgery (lobectomy, isthmusectomy, subtotal thyroidectomy). None of the patients had previous exposure of his or her neck to radiation, which increases the risk of thyroid carcinoma.

Diagnoses before surgery were euthyroid multinodular goitre (n = 653, 70.1%), toxic multinodular goitre (n = 81, 8.7%), Graves disease (n = 166, 17.8%) and recurrent goitre (n = 32, 3.4%) (Table 1). Of the 932 patients in the study cohort, 861 (92.4%) were referred by endocrinologists and family physicians, whereas 71 (7.6%) came directly for a surgical consultation.

The most common indications for surgery were multiple nodules involving both lobes (n = 578, 62%) and large or retrosternum goitre causing mechanical obstruction (n = 162, 17.4%). We observed tracheomalacia in only 2 patients (0.2%).

Altogether, 166 patients with Graves disease and 81 patients with toxic multinodular goitre, had been treated with 5 days after thyroidectomy in all patients.

Table 1. Benign thyroid diseases among 932 patients who underwent total thyroidectomy between 1985 and 2005

<table>
<thead>
<tr>
<th>Diagnosis (prior to surgery)</th>
<th>No. (%) of patients</th>
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<tbody>
<tr>
<td>Multinodular nontoxic goitre</td>
<td>653 (70.1)</td>
</tr>
<tr>
<td>Multinodular toxic goitre</td>
<td>81 (8.7)</td>
</tr>
<tr>
<td>Graves disease</td>
<td>166 (17.8)</td>
</tr>
<tr>
<td>Recurrent nodular goitre</td>
<td>32 (3.4)</td>
</tr>
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</table>
conservatively before surgery for a mean interval of 32.4 (range 10–290) months. As is common procedure, these 247 (26.5%) patients received antithyroid drugs alone (n = 157, 63.6%) or in combination with β-adrenergic blocking drugs (n = 88, 35.6%), or β-blockade alone (n = 2, 0.8%); 122 (49.4%) patients received antithyroid and/or β-blockade in combination with hormone substitution. The indications for total thyroidectomy in these 247 thyrotoxic patients were relapse of hyperthyroidism after medical treatment (n = 89, 36%), worsened endocrine ophthalmopathy with medical treatment (n = 27, 10.9%), side effects and subjective complaints of discomfort with medical treatment (n = 27, 10.9%) and large multinodular goitre (n = 104, 42.1%).

Among the subset of 166 thyrotoxic patients with Graves disease, the incidence of relapse of hyperthyroidism after medical treatment before surgery was 73.5% (46.9% within 6–18 months after discontinuation of medical treatment), and that of worsened endocrine ophthalmopathy with medical treatment before surgery was 16.3%. Additional indications for total thyroidectomy included refusal of radioactive iodine treatment (n = 27, 10.9%) because the patients feared exposure to radiation and/or wanted a rapid and permanent solution to symptoms.

The indications for completion thyroidectomy among the 32 patients with recurrent goitre after previous partial thyroidectomy were recurrence of hyperthyroidism (n = 2, 6.25%) and local recurrence of nodular disease involving one or both lobes (n = 30, 93.75%). According to available data, the method of previous thyroid resection was lobectomy in 15.6%, hemithyroidectomy (lobectomy and isthmusectomy) in 6.25% and subtotal thyroidectomy in 78.15%. The range of recurrence was 8–17 years; the rate of recurrence was higher among patients who had undergone subtotal thyroidectomy for benign nodular disease involving both lobes (46.9%).

The most common pathologies were benign multinodular goitre (n = 660, 70.8%), Graves disease (n = 164, 17.6%) and thyroid cancer other than microscopic papillary carcinoma less than 1 cm (n = 63, 6.8%), whereas the incidence of other less common benign conditions was 3.6%. Final pathology, including histologic subtypes of thyroid malignancy, is described in Table 2.

The average thyroid volume after total thyroidectomy was 80.8 (range 17.3–216) cm³, whereas the average volume of the resected gland with thyroid cancer (median diameter 1.27 cm) was 75.6 cm³.

Recurent laryngeal nerve palsy occurred in 14 patients (1.5%); permanent unilateral palsy occurred in 2 patients (0.2%). Both these patients had recurrent nodular disease after subtotal thyroidectomy for multinodular goitre. Temporary recurrent laryngeal nerve palsy, resolving within 2 months, occurred in 12 patients (1.3%). Temporary hoarseness was more common among patients with multinodular goitre compared with those who had Graves disease. We observed no temporary or permanent bilateral recurrent laryngeal nerve injury. In all patients, preoperative laryngoscopy showed normal vocal cord motility.

Hypocalcemia occurred in 71 patients (7.62%). The rate of temporary hypocalcemia was 7.3%; among these patients, 25 (2.7%) had temporary severe hypocalcemia and 43 (4.6%) had temporary nonsignificant hypocalcemia. Permanent hypocalcemia occurred in 3 (0.3%) patients.

Complications are described in Table 3. Temporary hypocalcemia was more common among patients with multinodular goitre, whereas temporary severe hypocalcemia was more common among patients with Graves disease than those with multinodular goitre. Permanent hypoparathyroidism occurred in 2 patients with large multinodular goitre and in 1 patient with Graves disease. Postoperative hemorrhage requiring surgical hemostasis occurred in 2 (0.2%) patients. Other postoperative complications included seroma in 3 (0.3%) patients. There was no postoperative mortality.

Table 2. Final pathology after total thyroidectomy for 932 patients who had surgery between 1985 and 2005

<table>
<thead>
<tr>
<th>Thyroid pathology</th>
<th>No. (%) of patients</th>
</tr>
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<tbody>
<tr>
<td>Benign multinodular goitre</td>
<td>660 (70.8)</td>
</tr>
<tr>
<td>Graves disease</td>
<td>164 (17.6)</td>
</tr>
<tr>
<td>Thyroid cancer</td>
<td></td>
</tr>
<tr>
<td>Total thyroid</td>
<td>63 (6.8)</td>
</tr>
<tr>
<td>Papillary</td>
<td>26 (2.8)</td>
</tr>
<tr>
<td>Follicular</td>
<td>27 (2.9)</td>
</tr>
<tr>
<td>Mixed type</td>
<td>7 (0.8)</td>
</tr>
<tr>
<td>Hurthle</td>
<td>3 (0.3)</td>
</tr>
<tr>
<td>Incidental microscopic papillary carcinoma</td>
<td>11 (1.2)</td>
</tr>
<tr>
<td>Other*</td>
<td>34 (3.6)</td>
</tr>
</tbody>
</table>

*Hashimoto thyroiditis, other thyroiditis, hydatid cyst, etc.

Table 3. Complications after total thyroidectomy among 932 patients who had surgery between 1985 and 2005

<table>
<thead>
<tr>
<th>Complication</th>
<th>No. (%) of patients</th>
</tr>
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<tbody>
<tr>
<td>Hypocalcemia</td>
<td></td>
</tr>
<tr>
<td>Total hypocalcemia</td>
<td>71 (7.62)</td>
</tr>
<tr>
<td>Temporary</td>
<td>68 (7.3)</td>
</tr>
<tr>
<td>Severe</td>
<td>25 (2.7)</td>
</tr>
<tr>
<td>Nonsignificant</td>
<td>43 (4.6)</td>
</tr>
<tr>
<td>Permanent</td>
<td>3 (0.3)</td>
</tr>
<tr>
<td>Recurrent laryngeal nerve palsy</td>
<td></td>
</tr>
<tr>
<td>Total recurrent laryngeal nerve palsy</td>
<td>14 (1.5)</td>
</tr>
<tr>
<td>Temporary</td>
<td>12 (1.5)</td>
</tr>
<tr>
<td>Unilateral</td>
<td>12 (1.3)</td>
</tr>
<tr>
<td>Bilateral</td>
<td></td>
</tr>
<tr>
<td>Permanent</td>
<td>2 (0.2)</td>
</tr>
<tr>
<td>Unilateral</td>
<td>2 (0.2)</td>
</tr>
<tr>
<td>Bilateral</td>
<td></td>
</tr>
<tr>
<td>Recurrent laryngeal nerve</td>
<td></td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>2 (0.2)</td>
</tr>
<tr>
<td>Seroma</td>
<td>3 (0.3)</td>
</tr>
</tbody>
</table>
During a median follow-up of 9 years, we observed no disease recurrence. All patients remained euthyroid with L-thyroxine supplementation.

At postoperative follow-up, serum calcium levels (9.4–10.2 mg/dL) were within the normal range. Temporary severe hypocalcemia, which occurred in 25 patients, resolved within 6 months (range of serum calcium levels was 7.8–9.2 mg/dL with 0.25–0.5 μg vitamin D and 2–3 g calcium daily). Among the 3 patients with permanent hypocalcemia, at the 1-year postoperative measurement serum calcium levels ranged from 7.9–8.8 mg/dL with vitamin D (0.5 μg daily) and calcium (1–2 g daily) supplementation.

**DISCUSSION**

Historically, the risks associated with major surgery to treat thyroid disease and the problems of adequate hormonal replacement deterred surgeons from performing total thyroidectomies. Although the procedure remains controversial it is increasingly being performed, and current indications include cancer, toxic and nontoxic multinodular goitre and Graves disease.1,3,9

When the thyroid is resectable at presentation, total thyroidectomy is the current treatment of choice for malignant disorders of the thyroid that follow either a less aggressive clinical course (e.g., papillary thyroid carcinoma) or a rapidly progressive course (e.g., anaplastic thyroid cancer).1,10–11

We, like many endocrine surgeons, consider total thyroidectomy to be a valuable surgical option for the management of several benign thyroid diseases, particularly among patients with an increased risk of recurrence. For instance, the use of total thyroidectomy among patients with Graves disease is controversial owing to the extent of resection; however, research in this area has indicated that a more radical resection is beneficial to such patients. Total thyroidectomy, therefore, is now recommended for these patients because it eliminates the source of the Graves disease autoantibodies; it eliminates the risk of disease recurrence; hypothyroidism is predictable and controllable by immediate thyroxine replacement; it alleviates any associated endocrine ophthalmopathy in 80%–85% of patients; and the risk of malignancy among patients with Graves disease is only about 4%, although the incidence can increase to 15% if cold nodules are present.15–16 Moreover, the risk of postoperative complications to the recurrent laryngeal nerve and parathyroid glands is equivalent for total and subtotal thyroidectomy.1,9

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.1,13–15 The advantages of total thyroidectomy in such cases are the prompt relief of symptoms; provision of a definite 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 (23%–45%) that is not treatable by thyroxine suppression therapy and will, therefore, involve repeat surgery.1,2,9 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.9

High complication rates of total thyroidectomy (hypoparathyroidism and recurrent laryngeal nerve palsy) have been reported in some case studies,12,22 whereas in many other studies the reported incidence has been low. Gough and Wilkinson1 reported recurrent laryngeal nerve palsy and permanent hypoparathyroidism following total thyroidectomy at the rates of 0.7% and 2.2%, respectively. Perzik11 reported an incidence of nerve injury of only 0.4% and no hypoparathyroidism. Similar low rates of permanent complications associated with total thyroidectomy have been reported in other studies.1,4,5,24–26 In addition, several studies reported no significant difference in complication rates among patients undergoing total thyroidectomy compared with those undergoing subtotal thyroidectomy.4,5 Complication rates were shown to be higher after total thyroidectomy when the surgery was performed by surgeons who were not specialized in endocrine surgery.1,2,5,26 Moreover, repeat surgery for recurrent thyroid disease carries significantly higher risks than the initial surgery,1,2,25–27 with the incidences of recurrent laryngeal nerve palsy and permanent hypoparathyroidism as high as 20.0%25 and 3.4%,27 respectively.

The proportion of total thyroidectomies compared with the total number of thyroid surgeries being performed has increased significantly in recent years.1 Our data suggest that total thyroidectomy can be carried out with minimum morbidity among patients with benign thyroid conditions, including multinodular goitre and Graves disease, when surgery is indicated. In our study, permanent unilateral recurrent laryngeal nerve injury and hypoparathyroidism occurred in only 0.3% and 0.2% of patients, respectively. Identification of laryngeal nerves during mobilization and dissection of thyroid lobes helped to prevent accidental injury, and visualization of the 4 parathyroid glands and preservation of their blood supply minimized inadvertent damage to these structures.

We agree with other authors that hemostasis can be better achieved with total thyroidectomy.27,28,30 In our study, postoperative hemorrhage requiring reoperation occurred in 2 patients (0.2%); the bleeding source was from branches of the inferior thyroid artery in 1 patient and from branches of the middle thyroid vein in the other patient. There was no wound infection, and prophylactic antibiotics were not used in our study.
CONCLUSION

Total thyroidectomy can be undertaken safely 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 or hemithyroidectomy. Moreover, complication rates decrease as the surgeons’ skills increase. As a result, total thyroidectomy is now widely accepted for the management of both malignant and benign thyroid disease.

Our data support that total thyroidectomy is a valuable option, when surgery is indicated, for treating benign thyroid conditions such as multinodular goitre and Graves disease. 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, although the risk is low. In such patients total thyroidectomy offers a definite management of thyroid cancer.

Long-term euthyroidism after total thyroidectomy is achieved easily with l-thyroxine supplementation, while cosmetic outcome is good with patient satisfaction and acceptance.

Competing interests: None declared.

Contributors: Drs. Efremidou, Liratzopoulos and Manolas designed the study. Drs. Papageorgiou and Liratzopoulos acquired the data, which Drs. Efremidou, Papageorgiou and Manolas analyzed. Drs. Efremidou and Papageorgiou wrote the article, which Drs. Liratzopoulos and Manolas reviewed. All authors provided approval for publication.

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