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Patient outcomes following thyroid surgery for thyrotoxicosis

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Ethical Standards

The study and manuscript adhere to the STROBE reporting guidelines for observational studies

Competing Interest Statement

There are no known competing interests with this project to declare

Abstract

Introduction:

Total thyroidectomy can be used as a definitive treatment modality for thyrotoxicosis. We aim to assess the outcomes of patients that were treated with surgery at a single secondary care site.

Method:

Retrospective cohort study analysing consecutive patients undergoing thyroid surgery for thyrotoxicosis between 24/11/2000 and 26/04/2019 (n=595).

Results:

Total thyroidectomy was performed in 95.4% of patients. Two-thirds of patients had Graves' histology. 22.8% became transiently hypothyroid whilst being on levothyroxine replacement. Transient and persistent hypocalcaemia was present in 23.3% and 2.8% respectively. Recurrent laryngeal nerve palsy was transient and persistent in 3.6% and 0.3% respectively. 2.5% of patients developed post-operative haematomas that required surgical evacuation in the operating theatre.

Conclusion:

The overall complication rate for thyroid surgery in thyrotoxicosis is higher than in euthyroid patients. Total thyroidectomy compared to other treatment modalities appears to be the most effective definitive management of Graves' disease

Keywords: thyrotoxicosis; thyroidectomy, complications

Introduction

Thyrotoxicosis is a disease characterised by inappropriately high levels of thyroid hormone acting at tissue level¹. This can be due to activation at any level of the hypothalamic-pituitary-thyroid axis. It predominantly affects women and is most commonly associated with Grave's disease or autoimmune hyperthyroidism².

Thyrotoxic patients can be treated medically in the first instance with thionamide therapy unless contraindicated to achieve remission. Once in remission, patients can be treated definitively by means of surgery, a time-limited course of thionamides, or radioiodine treatment. The American Thyroid Association (ATA) published guidelines in 2016 where any three of those modalities may be considered as first-line treatment depending on the patient's circumstances and values³.

Surgery in the thyrotoxic patient can be challenging for several reasons. This is reflected by a higher complication rate than for those who are euthyroid. In a metabolically overactive gland, an increased blood supply can lead to more intra-operative bleeding as well as an increased post-operative haematoma risk. Pankhania et al (2017) analysed 1280 patients undergoing thyroid surgery at a single tertiary centre. They found a 1.35% return-to-theatre rate for postoperative haematoma in non-Graves' patients but an overall 2.11% return-to-theatre rate when Graves' patients were included due to an almost four times higher return rate in Graves' patients⁴. Other anaesthetic considerations include an increased risk of cardiac arrhythmias and thyroid crisis. Additionally, post-operatively thyrotoxic patients are at increased risk of hypocalcaemia due to hypoparathyroidism.

Thionamides can achieve long-term remission rates of 35%, however, thionamide therapy has a significant side effect profile and remission is only achievable in cases of Grave's disease⁵.

A single cycle of radioiodine can achieve excellent results (>90%)⁶ in the long-term control of thyrotoxicosis and so thyroid surgery is frequently reserved for selected patients. These are typically

those who cannot be rendered euthyroid by other means, have significant ophthalmopathy, or have contraindications for radioiodine such as women planning pregnancy.

The multidisciplinary thyroid clinic in Hull Royal Infirmary comprises a joint clinic run by endocrinologists and ENT surgeons together. All patients who present with thyrotoxicosis, where possible, are initially controlled with thionamide therapy and are then given the option of each of the three definitive treatment modalities (as well as the option of lifelong thionamide therapy) with audited risks and benefits of each option explained. In our experience, when patients are given the option, a large number of them will opt for surgery as first-line definitive treatment over the other treatment modalities. As a result of this, we believe our case series is one of the largest of thyrotoxic patients undergoing thyroid surgery. We aim to compare outcomes and complication rates to the literature.

Materials and Methods

Reporting standards

This study and manuscript adhere to the STROBE reporting guidelines for observational studies⁷.

Data were collected retrospectively and entered into Excel workbooks (Microsoft Office 365, Microsoft, Redmond, WA, USA).

Patients were pseudo-anonymised and given a unique study number. Demographic data such as age at operation, sex and family history were recorded.

Data was gathered using the electronic medical record solution, Evolve 3 (Kainos, Belfast, Northern Ireland) and Lorenzo patient record systems (DXC Technology, Virginia, United States). For laboratory data, Integrated Clinical Environment (ICE) was used (EMIS Health, Leeds, United Kingdom).

We recorded the referral source, any relevant clinical findings, the type of operation (mainly total thyroidectomy or hemithyroidectomy), histology of the gland, and the presence or absence of

postoperative complications. These included: recurrent laryngeal nerve palsy (post-operatively and at three months follow-up), hypocalcaemia, wound infection, and haematoma.

Biochemical markers were recorded pre-and post-operatively. These included thyroid-stimulating hormone (TSH), free-thyroxine (T4), and adjusted serum calcium.

Results

A total of 595 patients (n=595) underwent a hemithyroidectomy or total thyroidectomy for thyrotoxicosis between 24/11/2000 and 26/04/2019 at a single secondary care site in the Yorkshire and Humber Deanery of Health Education England. All operations were performed by the same surgeon.

The mean age was 44 years. As expected, there was a female preponderance with a female to male ratio of 4.5:1.

Operation type

The majority of patients, 95.4% (n=568) underwent a total thyroidectomy. Two of those had an additional parathyroidectomy and one was a revision total thyroidectomy. Hemithyroidectomies were performed in 4.5% (n=27) including two revision hemithyroidectomies. None of the patients in this cohort had subtotal thyroidectomies.

Histology

The histology was accessible in 87.7% (n=522) of the patients. As compared to the literature², two-thirds of cases, 66.7% (348/522), were autoimmune hyperthyroidism or Grave's disease. 8.2% (n=43) cases were histologically Hashimoto's thyroiditis. A full breakdown of the remaining histological subtypes is available in Table 1. We found 6.1% (n=32) of the patients had evidence of microcarcinoma, normally papillary thyroid cancer. One of the patients whose histology showed Grave's disease had a rare case of struma ovarii.

Table 1. A table showing the histological findings of the thyroid glands post-operatively

TSH and T4

Biochemical markers were measured at the point of referral to ENT and again pre-operatively. Our data set was able to record these values from 2007 onwards (n=338) as the historical data was unavailable electronically.

As expected, at the point of presentation or referral to ENT for consideration of surgery, most patients (72.5%, n=245) had maximally suppressed TSH, defined as <0.05 mIU/L. Only 1.5% (n=5) of patients had raised TSH levels >5mIU/L. 39.3% (n=133) of the patients had suppressed levels of TSH at the point of surgery compared to the initial presentation.

A known consequence of thyroid surgery is hypothyroidism and this is substituted with lifelong L-thyroxine for those who had total thyroidectomies. 22.8% (n=77) patients became transiently hypothyroid post-operatively whilst on T4 replacement, with TSH levels ranging from 5.3 – 83 mIU/L. Of note, the patient whose TSH level was the highest in the cohort had been non-compliant with their medication for over one year. Our T4 replacement dosage is calculated on an individual patient basis using the regression equation; weight (kg) – age + 125 mcg/day⁸. Dose alteration or education in the avoidance of simultaneous polypharmacy when taking thyroxine was required in these patients.

Post-operative adjusted calcium levels

All patients undergoing total thyroidectomy underwent routine postoperative calcium monitoring. According to the British Association of Endocrine and Thyroid Surgeons (BAETS) algorithm⁹, serum adjusted calcium was defined as hypocalcaemia of less than 2.10 mmol/L. Post-operative calcium level checks were performed at 9:00 am the following day and again at 3:00 pm. Both levels were accessible on the electronic records in 288 cases.

The mean initial post-operative serum adjusted calcium was 2.21 mmol/L (range 1.63 – 2.55mmol/L). 20.8% (n=60) of patients had an initial post-operative hypocalcaemia (1.63 mmol/L – 2.09 mmol/L; mean 1.99mmol/L).

The second calcium level check mean was lower at 2.19mmol/L (range 1.75 – 2.60 mmol/L) and an additional seven patients (n=67) were hypocalcaemic on the second check. Follow-up calcium levels were available in 135 patients – this was typically recorded at a three-month follow-up. These were only available in patients still requiring calcium and/or vitamin D supplementation. Only eight patients remained hypocalcaemic at this point. The rate of transient hypocalcaemia, therefore, was 23.3% (67/288) and persistent hypocalcaemia 2.8% (8/288).

Post-operative recurrent laryngeal nerve palsy

A recognised complication of thyroid surgery is recurrent laryngeal nerve palsy which may be temporary or permanent. In our cohort, 3.6% (n=12/329) patients had an early recurrent laryngeal nerve palsy on flexible laryngopharyngoscopy. Of these, only 0.3% (n=1) had a palsy still present at a three-month follow-up; the remainder were transient and had recovered.

Post-operative haematomas and seromas

In our cohort, we had 2.5% (n=15) documented postoperative haematomas which required drainage in theatre. Three patients developed seromas and 2 separate patients underwent scar excision for scar hypertrophy.

Other complications

One patient had a laryngeal tear and a concurrent early recurrent laryngeal nerve palsy which recovered at three months post-surgery. The patient with struma ovarii had a subsequent hysterectomy.

Discussion and Conclusions

As compared with the literature, the common demographics for thyrotoxic patients are the same. Our most prevalent histology was Graves' disease, followed by multi-nodular goitre and Hashimoto's thyroiditis.

Our overall rate of malignancy was 15.3% with papillary thyroid cancer being the most common. The same observation was made in a systematic review of the incidence of thyroid carcinoma in patients undergoing thyroidectomy for thyrotoxicosis, where the overall rate of malignancy was 8.5% and the most common histology was micropapillary carcinoma¹⁰. Careful pre-operative assessment of any nodules is important as they are associated with an increased risk of thyroid cancer in patients undergoing thyroidectomy for thyrotoxicosis¹¹.

The overall complication rate for thyroid surgery in thyrotoxicosis is higher than in euthyroid patients. Whilst transient post-operative complications such as hypocalcaemia or recurrent laryngeal nerve palsies were present in 23.3% (67/288) and 3.6% (12/329) respectively, the persistence of these symptoms was much lower at documented outpatient follow-up.

In a systematic review and meta-analysis of the predictors of post-thyroidectomy hypocalcaemia, two factors associated with transient hypocalcaemia were Graves' disease and female sex¹². These factors are heavily relatable in our study as 67.1% of those with hypocalcaemia had Grave's aetiology and 87.7% were female.

Graves's disease is a known risk factor for neck hematoma requiring surgical intervention^{13,14}.

Consequently, with the majority of our population study being Graves' disease and undergoing total thyroidectomy, our 2.5% post-operative haematoma was expected.

Comparison to other studies

Whilst there are several larger studies assessing incidence of thyroid carcinoma in patients undergoing total thyroidectomy for hyperthyroidism¹⁰, we aim to compare our data with the literature assessing whether surgery remains a safe modality for the treatment of thyrotoxicosis.

Shinall MC et al (2013) assess 165 patients undergoing total thyroidectomy for Graves' disease where 42% of the cohort remained hyperthyroid at the time of surgery. They found temporary and permanent hypocalcaemia rates of 31% and 1.2% of their cohort respectively. Temporary and permanent recurrent laryngeal nerve palsies were present in 7% and 0.6% respectively. Multivariate analysis was performed which demonstrated patient age <45 years and obesity were associated with occurrence of complications¹⁵.

Ali A et al (2019), assess for complications and outcomes undergoing total thyroidectomy following rapid control of thyrotoxicosis compared to those in well-controlled disease¹⁶. 266 patients were included with similar demographic data to our study. Of those, 19 patients had poorly controlled disease after rapid optimisation. Long term hypoparathyroidism occurred in 4.9% and recurrent laryngeal nerve palsy in 0.38%. Our cohort, whilst larger, experienced fewer proportional complications of hypocalcaemia and recurrent laryngeal nerve palsies than both of these comparative studies.

Despite the drawbacks of retrospective analysis, this large cohort still suggests that thyroid surgery has a useful role in the management of refractory hyperthyroidism. In particular, total thyroidectomy compared to other treatment modalities appears to be the most effective definitive management of Graves' disease¹⁷. Moreover, a meta-analysis suggested higher relapse rates with antithyroid medications than surgery in Graves's disease patients¹⁸.

- Thyrotoxic patients can be treated medically in the first instance, unless contraindicated, to achieve remission
- Patients can then be treated definitively by surgery, a time-limited course of thionamides, or radioiodine treatment
- A single cycle of radioiodine can achieve excellent results in the long-term control of thyrotoxicosis and so surgery is frequently reserved for selected patients
- Complication rates, such as post-operative haematoma, hypocalcaemia or recurrent laryngeal nerve palsy for thyrotoxic patients are higher than in euthyroid patients

- Long term complications rates for hypocalcaemia and recurrent laryngeal nerve palsy still remain relatively low
- This large cohort study confirms that total thyroidectomy still has a useful role for refractory hyperthyroidism
- Total thyroidectomy compared to other treatment modalities appears to be the most effective definitive management of Graves' disease

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Table 1. A table showing the histological findings of the thyroid glands post-operatively

Histology	Number of cases
Papillary thyroid cancer + hyperplasia	1
B cell lymphoma	1
Follicular adenoma	11
Nodular hyperplasia	7
Follicular carcinoma	2
Follicular adenoma + multinodular goitre	5
Follicular adenoma + papillary thyroid cancer	1
Follicular adenoma + multinodular goitre + papillary thyroid cancer	1
Graves	326
Graves + papillary thyroid cancer	12
Graves + nodular hyperplasia	1
Graves + Hurthle cell	1
Hashimotos + papillary thyroid cancer	5
Hashimotos	40
Hurthle cell	1

Multi-nodular goitre	87
Multi-nodular goitre + follicular adenoma	4
Multi-nodular goitre + papillary thyroid cancer	6
Nodular hyperplasia + papillary thyroid cancer	1
Grave's + follicular adenoma	8
Hurthle cell + papillary thyroid cancer	1