

Long-term outcomes after total thyroidectomy

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ABSTRACT

INTRODUCTION: The aim of this study was to assess the complication rates of total thyroidectomy in a regional hospital setting in Denmark for permanent hypoparathyroidism, recurrent laryngeal nerve palsy and post-operative bleeding. Furthermore, the long-term outcomes in the management of hypoparathyroidism were investigated.

METHODS: This was a retrospective study of 114 consecutive patients undergoing total thyroidectomy due to benign thyroid disease.

RESULTS: A total of 0.9% suffered from permanent recurrent laryngeal nerve palsy, whereas temporary nerve palsy was seen in 1.8%. Post-operative bleeding occurred in 5.4%. The frequencies of temporary and permanent post-operative hypocalcaemia were 22.8% and 17.4%, respectively. Autotransplantation of parathyroid tissue was performed in 23.7%. Unintentional parathyroidectomy occurred in 8.7%. Serum ionized calcium was significantly lower preoperatively in the group that developed hypocalcaemia ($p = 0.03$).

CONCLUSIONS: The incidence of recurrent laryngeal nerve palsy was similar to that reported in other published studies. Post-operative bleeding was more common than in other studies. The high frequency of permanent post-operative hypocalcaemia is a cause for concern. We need to consider implementing a guideline to facilitate out-facing calcium and vitamin D supplements as an attempt to phase out was not attempted in all patients.

FUNDING: not relevant.

TRIAL REGISTRATION: The study was approved by the Danish Data Protection Agency, but has not been registered due to its register-based design.

and post-operative bleeding at 1.69, 1.85 and 2.58, respectively [4].

The shift towards more radical thyroid surgery is justified by notable recurrence rates of the goitre (9-43%) and an increased risk of post-operative complications in re-operations [1].

Chronic hypoparathyroidism results from unintentional extirpation of parathyroid tissue during surgery or from interruption of the blood supply to the glands, which causes infarction. Signs and symptoms of hypocalcaemia include paresthesia, muscle cramping and convulsions.

RLN injury manifests as hoarseness, weakness and breathiness of the voice and occurs in 0-14% of cases after total thyroidectomy [5].

The main challenge of thyroid surgery is to cure the problems caused by the thyroid disease while keeping the complications to an absolute minimum, particularly when dealing with benign thyroid disease.

Few studies report long-term calcium problems after total thyroidectomy on benign indication [3, 4, 6-10].

The aim of the present study was to assess the complication rates of total thyroidectomy on benign indication and first-time thyroid surgery in a regional hospital setting in Denmark regarding permanent hypocalcaemia, RLN palsy and post-operative bleeding. Furthermore, long-term outcomes in the management of hypocalcaemia were investigated.

METHODS

We conducted a retrospective review of 114 consecutive patients who underwent total thyroidectomy over the six-year period from January 2006 to December 2011 at the Department of Otolaryngology, Slagelse Hospital, Denmark. We extracted data on sex, age, histopathology, hypocalcaemia, parathyroid autotransplantation, RLN palsy and post-operative bleeding. The patients were found by a search based on the surgical procedure code (KBAA60); these data were cross-checked with the national Thykir database, which contains information on all thyroid procedures performed within the specialty of ENT Head and Neck Surgery in Denmark since 2001. We excluded patients with thyroid cancer and patients who had previously undergone thyroid surgery to make the results comparable with previously published studies with these criteria.

ORIGINAL ARTICLE

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Dan Med J
2015;62(11):A5156

Recent decades have seen an increasing trend towards more radical surgery in benign thyroid surgery, i.e. total or hemithyroidectomy instead of subtotal resection [1, 2]. The main causes of concern in thyroid surgery are chronic hypoparathyroidism and recurrent laryngeal nerve (RLN) palsy. Another complication of thyroid surgery is the risk of post-operative bleeding, which can be life-threatening due to respiratory obstruction [3].

In a published meta-analysis, these complications were reported to be higher when performing total rather than hemithyroidectomy [4]. Total thyroidectomy had a higher pooled relative risk (RR) for temporary and permanent hypocalcaemia at 10.67 and 3.17, respectively. Furthermore, total thyroidectomy had a higher pooled RR for temporary and permanent RLN palsy

Using PubMed and the following MeSH words “total thyroidectomy”, “benign”, “complications” and “hypocalcaemia”, we found 101 articles and selected those that were relevant.

Preoperative assessment

T3, T4, TSH and Ca^{2+} were measured. To exclude pre-existing vocal cord palsy, vocal cord motility was assessed preoperatively.

Routine measurements of serum parathyroid hormone and phosphate were not performed.

Surgical procedure

Surgery was performed with conventional instruments and bipolar electrocoagulation. Identified parathyroid glands were preserved together with their blood supply if detected and if possible. When a parathyroid gland was devascularised, autotransplantation into the ipsilateral sternocleid muscle was performed. The RLN nerves were always identified, and care was taken to avoid injury to these nerves. A nerve stimulator was used, but nerve intraoperative monitoring was not used. Drains were not routinely used in these operations and were only placed on indication at the surgeon's discretion, e.g. a drain was placed when a large goitre weighing more than 200 g was removed.

Post-operative management

Ca^{2+} was measured on the day of surgery and three times daily on subsequent days until two consecutive, stable or increasing values had been achieved.

The 1.15–1.35 mM range was defined as the normal range for Ca^{2+} . Treatment against hypocalcaemia with a calcium supplement was started if symptomatic or if Ca^{2+} dropped below 1.0 mM, which therefore was the measure of hypocalcaemia. If continuously symptomatic or if Ca^{2+} continued to decline despite this treatment, a vitamin D analogue was added.

RLN palsy was defined as hoarseness associated with vocal cord paralysis. All patients underwent indirect laryngoscopy or fibrelaryngoscopy before discharge.

Hormonal replacement therapy with L-thyroxine was initiated on the night of the operation.

Follow-up

All patients were seen for an otolaryngological post-operative follow-up a few weeks after surgery. In case of RLN palsy, the patients were evaluated by otolaryngologists every three months post-operatively. After one year, the palsy was considered permanent.

Hormonal replacement therapy with L-thyroxine and treatment of hypocalcaemia were controlled by endocrinologists.

The overall median follow-up period was 13 months

(range: 1–56 months), whereas the median follow-up period in the hypocalcaemic group was 23 months (range: 5–56 months). One patient ended the endocrinological follow-up after five months. A one-year Ca^{2+} measurement was available, and the patient was therefore controlled elsewhere.

Information to establish if the patients picked up their prescriptions was extracted from the receipts database.

Statistics

Statistical analysis was performed using SPSS for Mac (version 19; SPSS Inc., Chicago, IL, USA). The non-parametric Kruskal-Wallis test was used to test for differences between groups.

The level of significance was defined as $p < 0.05$.

Trial registration: The study was approved by the Danish Data Protection Agency (R. no. 2008-58-0020), but has not been registered owing to its register-based design.

RESULTS

Of the 114 patients, 99 were females (86.8%) and 15 were males (13.2%). The median age was 50 years (range: 19–80 years).

Histopathologic diagnoses are presented in **Table 1**. 2.7% suffered from unilateral RLN palsy. 1.8% recovered fully from their palsy within six months and were therefore classified as temporary palsies. 0.9% had not recovered after one year, and the palsy was therefore considered permanent.

5.4% had surgery for haemostasis. All cases of post-operative bleeding occurred within 24 hours after surgery.

Details on post-operative hypocalcaemia are outlined in **Table 2**. In the group of patients classified with permanent hypocalcaemia, phasing-out of calcium or calcium and vitamin D had never been attempted in three of these patients. Another interesting finding was that six of the nine patients who should be taking vitamin D supplements, according to their medical file, had not picked up their prescription for a minimum of two years (Table 2).

A variable number of parathyroid glands were subjectively identified by the surgeon (**Table 3**). Autotransplantation of parathyroid tissue was performed in 23.7% of cases and this was significantly associated with a lower Ca^{2+} level at day 1 and day 2 post-operatively ($p = 0.01$ and $p = 0.02$), but not after one year ($p = 0.32$). Unintentional parathyroidectomy occurred in 8.7% as reported in the pathology reports.

We found no statistically significant differences between the Ca^{2+} level and histopathological diagnosis, post-operative bleeding, palsy or the number of para-

thyroid glands seen peroperatively. Ca^{2+} levels were lower in the group treated for hypocalcaemia at all times. However, we found that Ca^{2+} was significantly lower preoperatively, also in the group that developed hypocalcaemia ($p = 0.02$).

DISCUSSION

Recurrent laryngeal nerve palsy

The incidence of RLN injury varies considerably in the literature. Rates from 0 to 14% have been published [5]. However, most studies present frequencies around 1% for unilateral RLN palsy and below 1% for bilateral RLN palsy [3, 6-8, 11-13]. In our study, one patient sustained a permanent RLN palsy which reduced the frequency to 0.9% in our study. No patients suffered from bilateral RLN palsy. Two patients (1.8%) developed transient RLN palsy. These results are in agreement with previously published studies [3, 6-8, 11-13].

Post-operative bleeding

The frequency of post-operative bleeding in our study was 5.4%. This is higher than reported in other published studies on total thyroidectomy which present frequencies in the 0.9-2.1% range [3, 6, 8, 11, 14]. Drainage is not standard procedure at our centre. This raises the discussion of drainage as a standard part of this kind of surgery. In three studies, it is unclear whether or not drains were applied [3, 6, 11]. In the study by Serpell et al [8], based on 336 total thyroidectomies, the incidence of post-operative haematoma was 0.9%, which was the lowest incidence presented in the literature. A randomised study including 116 patients [14] examined the use of drainage after total thyroidectomy. The authors concluded that post-operative haematomas could not be prevented by the use of drainage. Furthermore, patients in whom drain was used had a significantly higher visual analogue scale score and required significantly larger amounts of post-operative analgesics. Some of these findings are in agreement with a Danish study from 2009 examining the frequency of post-operative bleeding after thyroid surgery [15]. This study included hemi- and total thyroidectomy due to benign as well as malignant pathology. The authors found an overall frequency of post-thyroidectomy bleeding of 4.2% and did not find that drainage reduced the post-operative bleeding frequency. The high incidence of post-operative haematomas in our study is a cause for concern. Whether or not applying drainage may lower the incidence of such haematomas remains unsettled according to the literature. A Cochrane study on wound drains following thyroid surgery also supports this conclusion, stating that there is no obvious, significant advantage associated with the use of drains after thyroid operations [16].

Post-operative hypocalcaemia

Surprisingly few studies report long-term calcium results after total thyroidectomy. In our study, 22.8% suffered from immediate post-operative hypocalcaemia. At the one-year follow-up, this number had decreased to only 17.4%. Other studies show immediate post-operative incidences in the 6.2%-35% range and follow-up incidences between 0% and 6% [3, 6-11]. Our high number of permanent hypocalcaemia is partly due to the fact that no attempt is being made to phase-out calcium and/or vitamin D.

In Denmark, post-operative treatment and regulation of thyroid medication as well as hypocalcaemia are controlled by endocrinologists. These findings could indicate the need for a discussion of the need for a guideline in order to ensure proper management of the phas-



TABLE 1

Histopathologic diagnosis of 114 patients undergoing total thyroidectomy.

Histopathology	Patients, n (%)
Nodular goitre with/without adenoma	98 (86)
Hyperplasia	12 (10.4)
Hashimoto's thyroiditis	3 (2.7)
Oncocytoma	1 (0.9)



TABLE 2

Distribution of post-operative hypocalcaemia in 114 patients undergoing total thyroidectomy.

Hypocalcaemia	Patients, %
Immediate	22.8
Permanent ^a	17.4
Not attempted outpaced	2.7
Not picked up vitamin D	5.4

a) Including those not attempted outpaced and those who have not picked up their vitamin D prescription.



TABLE 3

Number of parathyroid glands identified peroperatively in 114 patients undergoing total thyroidectomy.

Parathyroid glands, n	Patients, n (%)
0	0
1	0
2	18 (15.8)
3	26 (22.8)
4	69 (60.6)
5	1 (0.9)

ing-out of calcium and/or vitamin D supplements after total thyroidectomy.

An important point to keep in mind when attempting to compare these studies is that every study has its own definition of hypocalcaemia and its own limit for when to start calcium and vitamin D supplementation. Furthermore, some published studies do not define when post-operative hypocalcaemia reaches a point that demands treatment. This makes it difficult to compare results between studies.

Parathyroid gland autotransplantation

Autotransplantation of parathyroid tissue was performed in 23.7%, which is a high percentage compared with the percentages reported in other published work (range: 3.1-22.1%) [3, 10, 11]. When reviewing pathology reports, we found a frequency of unintentional parathyroidectomy of 8.7%. This frequency is rarely published, and it is therefore difficult to conclude anything from this figure. One study published a frequency of 5.2% [10].

We found that when autotransplantation was performed, Ca^{2+} levels were only significantly lower on the first and second post-operative day, and that autotransplantation did not lead to a significantly higher number of patients leaving the hospital while receiving treatment for hypocalcaemia. However, it remains unclear whether this is owed the fact that the glands that were not transplanted were functioning well, and that autotransplantation is therefore unnecessary.

We found no statistically significant differences between post-operative Ca^{2+} levels and the number of parathyroid glands seen peroperatively ($p > 0.12$).

Preoperative Ca^{2+} level a predictor for development of hypocalcaemia?

Preoperative Ca^{2+} levels were significantly lower preoperatively in the group that developed post-operative hypocalcaemia ($p = 0.02$). To our knowledge this is a novel finding that may prove worthy as a predictor in the development of post-operative hypocalcaemia. We did not have vitamin D measurements on these patients and therefore cannot establish their potential preoperative vitamin D insufficiency. This needs to be examined in future studies.

CONCLUSIONS

The incidence of RLN palsy in our study is similar to that reported in other published studies. Post-operative bleeding was more common than in other published studies. The high incidence of hypocalcaemia one year after surgery is a cause for concern. However, we did find that phasing out of calcium and/or vitamin D supplements had not been attempted in all patients, and not all patients picked up their vitamin D prescriptions,

which suggest a lower incidence of permanent hypocalcaemia. This indicates a need for a more structured approach to the phasing out of calcium and/or vitamin D.

Perspective: parathyroid hormone as a predictor of development of post-operative hypocalcaemia

In recent years, measurement of parathyroid hormone (PTH) in the blood has increasingly been used to predict which patients will suffer from post-operative hypocalcaemia. Grodski et al published a review on this in 2008 [2]. They concluded that post-thyroidectomy PTH levels accurately predict hypocalcaemia, but lack 100% accuracy. This is due to the fact that 5-10% will develop hypocalcaemia despite a normal PTH [17]. However, severe hypocalcaemia is unlikely when PTH is normal, and if symptoms appear they can be treated with over-the-counter oral calcium supplements [17]. Post-operative PTH measurement can be taken from ten minutes post-operatively to several hours later. Few thyroid surgery centres in Denmark measure PTH routinely to facilitate early treatment with calcium and/or vitamin D supplements. We believe that it should be standard protocol in Denmark to measure pre- and post-operative PTH in order to reduce cases of severe post-operative hypocalcaemia as well as to reduce length of hospital stay due to hypocalcaemia.

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ACCEPTED: 10 September 2015

CONFLICTS OF INTEREST: none. Disclosure forms provided by the authors are available with the full text of this article at www.danmedj.dk

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