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The long-term outcomes of thyroid function after subtotal thyroidectomy for Graves' hyperthyroidism

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ARTICLE INFO

Article history:
Received 14 April 2017
Received in revised form
22 June 2017
Accepted 29 June 2017
Available online xxx

Keywords:
Graves' disease
Hyperthyroidism
Subtotal thyroidectomy
Recurrence

ABSTRACT

Background: Surgical management of Graves' disease (GD) is changing from subtotal to total thyroidectomy because the latter eliminates the risk of recurrence. However, to preserve thyroid function in a euthyroid state, subtotal thyroidectomy is still performed for GD in non-Western countries. Therefore, we designed a study to investigate the long-term outcomes in GD patients after subtotal thyroidectomy and the correlation between remnant weight and postoperative thyroid function.

Materials and methods: This was a retrospective cohort observation study. Between January 2005 and December 2011, 415 consecutive GD patients treated by subtotal thyroidectomy were enrolled. All data were collected from 385 patients who underwent bilateral subtotal thyroidectomy and 57 patients who underwent the Hartley-Dunhill operation. The median postoperative follow-up time was 72 months (range 12-144 months).

Results: The mean weight of the preserved thyroid remnant was 5.1 g. Persistent or recurrent hyperthyroidism was observed in 119 (28.7%) patients. The median time of recurrence was 36 months (range 12-120 months). Hypothyroidism developed in over 50% of patients. A euthyroid state was achieved in only 19.3% of patients, and the rate did not increase significantly as remnant weight increased. Based on a Cox regression analysis, the remnant weight is an independent risk factor for persistent or recurrent hyperthyroidism (hazard ratio: 1.323, 95% confidence interval: 1.198-1.461, $P < 0.001$).

Conclusions: Subtotal thyroidectomy with the intent to maintain a euthyroid state is not an optimal surgical strategy for the definitive treatment of GD because the persistence or recurrence rate is high and the euthyroid rate is lower than expected.

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http://dx.doi.org/10.1016/j.jss.2017.06.091

Introduction

Graves' disease (GD), an autoimmune disorder, is the most common etiology for hyperthyroidism, accounting for 60%-80% of cases.[1] Currently, there are three treatment modalities for Graves' hyperthyroidism: antithyroid drugs (ATDs), radioactive iodine therapy, and thyroidectomy. Compared with the other modalities, thyroidectomy is the more consistently definitive therapy because it has the advantages of rapid remission and a high rate of curing the hyperthyroidism associated with GD.[2,3] According to the 2016 guidelines for the management of hyperthyroidism published by the American Thyroid Association, total thyroidectomy and near-total thyroidectomy are recommended as the surgical treatments for Graves' hyperthyroidism rather than subtotal thyroidectomy because total thyroidectomy eliminates the risk of recurrence,[4] whereas subtotal thyroidectomy leaves a chance of recurrence (ranging from 1% to 20%).[5] However, subtotal thyroidectomy with a remnant left on one or both sides is still the favored surgical procedure for treating GD in countries outside of the Western world because postoperative thyroid hormone replacement medications are not readily available.[6] Concerns regarding the necessity for lifelong hormone therapy may influence patients' perceptions in the choice of whether to undergo total thyroidectomy for a benign thyroid disease. With this background, we designed this study to investigate the long-term outcomes of patients with Graves' hyperthyroidism after subtotal thyroidectomy and the correlation between remnant weight and postoperative thyroid function. Furthermore, the possible risk factors of postoperative persistent or recurrent hyperthyroidism were analyzed and identified. Finally, we were interested in whether subtotal thyroidectomy would be a practicable surgical procedure for the treatment of GD in the modern era.

Materials and methods

Patients

This retrospective cohort observation study was approved by the Institutional Review Board (IRB) of the Chang Gung Medical Foundation, Taiwan (IRB Reference Number: 201601543B0). The IRB approval waived informed consent. Diagnoses of GD were made based on the symptoms/signs of hyperthyroidism, thyroid function test results, and the presence of serum antithyroid autoantibodies. Between January 2005 and December 2011, 629 patients diagnosed with GD underwent thyroid surgery at our institution. Only 13 patients underwent total thyroidectomy because of their preoperative diagnosis with a malignancy and recurrent hyperthyroid status after primary surgery. Patients without a postoperative follow-up or patients with incomplete thyroid function test results were excluded. Ultimately, 415 consecutive patients treated by subtotal thyroidectomy were enrolled, and all data from these patients were collected. The last doctor's visit was January 31, 2017. The median postoperative follow-up time was 72 months (range 12-144 months).

Surgical procedures

All patients received ATD therapy with or without β-adrenergic blockade to render them euthyroid before the surgical procedure. Subtotal thyroidectomy included two procedures: bilateral subtotal thyroidectomy (BST), with a remnant left on both sides, and the Hartley-Dunhill operation (HD), with a remnant left on one side. There were no definite criteria for patient selection for either BST or HD in our past practice during this study period. However, most surgeons performed HD if the patient had a preoperative sonography examination and definite nodular lesions were found or asymmetric enlargement of the unilateral thyroid lobe was noted. The thyroid remnant was located close to the Berry's ligament, and the blood supply from the inferior thyroid artery was preserved. The size of the remnant was judged by the operating surgeon based on his experience, the total size of the thyroid gland, and the degree of hyperthyroidism. Remnant weight was calculated based on its length X width X thickness in comparison with the resected thyroid specimen. Postoperatively, serum calcium levels and parathyroid hormone concentrations were measured at least once during hospitalization and were then followed intensively if there was evidence of hypocalcemia or hypoparathyroidism. Hypocalcemia was defined as a serum calcium concentration <8.0 mg/dL. Permanent hypoparathyroidism was defined as a serum parathyroid hormone concentration <14.0 pg/mL with a persistent requirement for medication to maintain normocalcemia over 6 months. If the patients had clinical or suspicious symptoms for recurrent laryngeal nerve (RLN) injury, the patients were referred to an otorhinolaryngologist for a laryngoscopic evaluation of vocal cord palsy. Permanent RLN injury was defined as persistent vocal cord palsy for over 6 months with no intervention.

Postoperative thyroid function follow-up

Follow-ups occurred at 1, 3, 6, and 12 months postoperatively and every 6 months thereafter and included measurements of serum triiodothyronine (T3) (reference range: 58-159 ng/dL), free thyroxine (FT4) (reference range: 0.76-1.64 ng/dL), and thyroid-stimulating hormone (TSH) (reference range: 0.35-5.50 uIU/mL). If the patient's thyroid function was maintained in a euthyroid state without any medication for 6 months, then the thyroid function test was performed every year. To evaluate changes in postoperative thyroid function, we classified hypothyroidism as clinical hypothyroidism (elevated TSH level with T3/FT4 levels below the normal range) and subclinical hypothyroidism (elevated TSH level with normal T3/FT4 levels) and hyperthyroidism as clinical hyperthyroidism (suppressed TSH level with T3/FT4 levels above the normal range) and subclinical hyperthyroidism (suppressed TSH level with normal T3/FT4 levels). Persistent hyperthyroidism, defined by a suppressed TSH level, was consecutively measured after surgery over 6 months within the first year. Recurrent hyperthyroidism was defined as a suppressed TSH level measured after 1 year after surgery and persisting for over 6 months.