



ORIGINAL ARTICLE

Predictive factors for intraoperative excessive bleeding in Graves' disease



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Summary *Background:* In Graves' disease, because a thyroid tends to have extreme vascularity, the amount of intraoperative blood loss (AIOBL) becomes significant in some cases. We sought to elucidate the predictive factors of the AIOBL.

Methods: A total of 197 patients underwent thyroidectomy for Graves' disease between 2002 and 2012. We evaluated clinical factors that would be potentially related to AIOBL retrospectively. *Results:* The median period between disease onset and surgery was 16 months (range: 1–480 months). Conventional surgery was performed in 125 patients, whereas video-assisted surgery was performed in 72 patients. Subtotal and near-total/total thyroidectomies were performed in 137 patients and 60 patients, respectively. The median weight of the thyroid was 45 g (range: 7.3–480.0 g). Univariate analysis revealed that the strongest correlation of AIOBL was noted with the weight of thyroid ($p < 0.001$). Additionally, AIOBL was correlated positively with the period between disease onset and surgery ($p < 0.001$) and negatively with preoperative free T4 ($p < 0.01$). Multivariate analysis showed that only the weight of the thyroid was independently correlated with AIOBL ($p < 0.001$). Four patients (2.0%) needed blood transfusion, including two requiring auto-transfusion, whose thyroids were all weighing in excess of 200 g. The amount of drainage during the initial 6 hours and days until drain removal was correlated positively with AIOBL ($p < 0.001$, each). Occurrences of postoperative complications, such as recurrent laryngeal nerve palsy or hypoparathyroidism, and postoperative hospital stay were not correlated with AIOBL.

Conclusion: A huge goiter presented as a predictive factor for excessive bleeding during surgery for Graves' disease, and preparation for blood transfusion should be considered in cases where thyroids weigh more than 200 g.

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1. Introduction

Graves' disease (GD) is an autoimmune disease, in which thyroid-receptor antibodies combine with the thyrotropin receptor, promoting the production of thyroid hormones in the follicular cells through stimulation of cyclic adenosine monophosphate.¹ GD is the most common cause of hyperthyroidism. Acceptable therapeutic options are antithyroid drugs (ATDs), radioiodine (RI) therapy, and surgery.^{1,2} The prevalence of therapy varies in different parts of world. ATDs are the first-line therapy in most of the Japanese patients, whereas RI is preferred in the United States.¹ Although the total number of patients in Japan who received RI therapy was much fewer than that in Europe or the United States,³ the application of RI therapy has extended due to the new regulation that allows its administration in outpatient clinics.⁴ Nevertheless, suspicion of malignancy, unwillingness to receive RI therapy, and pregnancy should still be good indications for surgery. Although thyroidectomy has been regarded as a prompt and assured therapy for GD, it has some drawbacks, such as operative scar, need for hospitalization, and complications related to operation, including recurrent laryngeal nerve (RLN) paralysis, hypoparathyroidism, and intraoperative bleeding.^{1,2} Especially in GD, the thyroid gland tends to have hypervascularity, and hemostasis is often difficult.^{5,6} In this study, we evaluated the factors that are relevant to the amount of intraoperative blood loss (AIOBL), and how AIOBL affects postoperative courses retrospectively.

2. Methods

We reviewed the clinical and laboratory data of 197 consecutive patients with GD, who underwent thyroidectomy between April 2002 and March 2012 at our department. Patients who had undergone neck surgery previously were excluded. GD was defined by the presence of thyrotoxicosis, a diffuse goiter, and a serum thyroid-stimulating hormone receptor antibody or thyroid-stimulating antibody. After the operation, the diagnosis was confirmed histologically in all patients. In preparation for surgery, all patients were given potassium iodide for a median period of 14 days. Operations were performed with conventional open surgery or video-assisted neck surgery. The indications and technique of video-assisted neck surgery were described previously.⁷ Subtotal thyroidectomy was defined as leaving between 2 g and 6 g thyroid tissue and near-total thyroidectomy was defined as leaving < 2 g thyroid tissue.

We placed closed suction drainage tubes prior to wound closure in all of the patients except one and removed them 1–3 days later. RLN injury was recorded if voice change was recognized. Calcium supplements and vitamin D analogs were given to those with symptomatic hypocalcemia. Patients who could discontinue the supplements after achieving normocalcemia within 12 months after surgery were identified as those with transient hypocalcemia, whereas patients who had to continue it for more than 12 months and continued to have a below-normal serum intact parathyroid hormone level were categorized as those with permanent hypoparathyroidism.

Clinical variables were assessed in relation to AIOBL. Univariate analysis was performed by single regression analysis to test the correlation between continuous variables and AIOBL, and Student *t* test was used to compare between groups. A *p* value of <0.05 was considered statistically significant. For multivariate analysis, the factors identified as being associated with $p \leq 0.10$ were entered into a stepwise regression analysis to determine the independent risk factors for AIOBL. Statistical analysis was performed with StatMate III for Macintosh (ATMS Co., Ltd, Tokyo, Japan).

3. Results

3.1. Background of patients and operative variables

Background of patients and operative variables are shown in Table 1. The majority were female (76.1%), with a median age of 34 years. The median period between the onset of the disease and operation was 16 months. The most frequent indication for operation was intolerance to ATDs (41.2%), followed by patient preference (25.4%) and uncontrollable disease (25.4%). Thirty-seven patients (18.8%) needed preoperative adrenocortical hormone administration due to an excessive value of serum-free T4 even after potassium iodide intake. Median intraoperative blood loss was 100 mL (range: 10–1390 mL), and four patients required blood transfusion. Thyroidectomy was performed by open surgery in 125 patients and video-assisted neck surgery in 72 patients. In terms of the extent of resection, 137 subtotal thyroidectomies and 60 near-total/total thyroidectomies were performed. The median weight of thyroid was 45 g (range: 7–480 g). Transient hypocalcemia was seen in 19.8% of the patients, but permanent hypoparathyroidism in only 1.0% of patients. RLN palsy was observed in 3.0% of patients, all of which were temporary. During the study period, we have not experienced hematoma requiring surgical evacuation. Patients were discharged after their operation within a median period of 4 days (range: 2–22 days).

3.2. Factors affecting AIOBL

Table 2 shows the correlations between clinical variables and AIOBL, as shown by univariate analysis. The strongest correlation of AIOBL was found with the weight of thyroid, with a correlation coefficient of 0.72 ($p < 0.0001$). Additionally, AIOBL was correlated positively with the period between disease onset and surgery (correlation coefficient 0.36, $p < 0.001$), and negatively with preoperative free T4 at the initial consultation (correlation coefficient -0.22 , $p < 0.01$). Multivariate analysis revealed that only the weight of the thyroid was correlated with AIOBL ($p < 0.0001$; Table 3). Out of four patients who needed intraoperative blood transfusion (Table 4), two underwent autotransfusion with preoperatively collected blood.

3.3. Impact of intraoperative blood loss on postoperative courses

Although AIOBL was correlated positively with the amount of drainage (correlation coefficient 0.47, $p < 0.0001$) and

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