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Original Research Article

Predictive factors for intraoperative excessive bleeding in Grave's disease

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ABSTRACT

Background: Grave's disease frequently results in and is the most common cause of hyperthyroidism. It also often results in an enlarged thyroid. It also known as toxic diffuse goiter, is an autoimmune disease that affects the thyroid. This study evaluates all the factors that cause intra-operative blood loss and how it affects the grave's disease.
Methods: This study was conducted on 100 patients with Grave's disease, who underwent thyroidectomy during the period from May 2010 to April 2016.
Results: The majority of patients were females which constitute about 76.3% with a median age of 33 years. The median period between the onset of the disease and operation was 15 months. Weight of thyroid in grams was 40. Post-operative hospital stay was 3 days. Univariate analysis revealed that the strongest correlation of amount of intraoperative blood loss (AIOBL) was noted with the weight of thyroid ($p<0.001$). Additionally, AIOBL was correlated positively with the period be- tween disease onset and surgery ($p<0.001$) and negatively with preoperative free T4 ($p<0.01$). Occurrences of postoperative complications, such as recurrent laryngeal nerve palsy or hypoparathyroidism, and postoperative hospital stay were not correlated with AIOBL.
Conclusions: For Grave's disease, for excessive bleeding during surgery, a large goiter presented as a predictive factor, and transfusion of blood should be considered in cases in which goiter weighs more than 200 g.

Keywords: Grave's disease, Intra-operative excessive bleeding, AIOBL

INTRODUCTION

Graves' disease, also known as toxic diffuse goiter, is an autoimmune disease that affects the thyroid.[1] It frequently results in and is the most common cause of hyperthyroidism. It also often results in an enlarged thyroid. Signs and symptoms of hyperthyroidism may include irritability, muscle weakness, sleeping problems, a fast heartbeat, poor tolerance of heat, diarrhea, and unintentional weight loss. Other symptoms may include thickening of the skin on the shins, known as pretibial myxedema, and eye bulging, a condition caused by Graves' ophthalmopathy. About 25 to 80% of people with the condition develop eye problems. The exact cause is unclear; however, it is believed to involve a combination of genetic and environmental factors.[2] A person is more likely to be affected if they have a family member with the disease. If one twin is affected, a 30% chance exists that the other twin will also have the disease. The onset of disease may be triggered by stress, infection, or giving birth.[3] Those with other autoimmune diseases such as type 1 diabetes and rheumatoid arthritis are more likely to be affected. Smoking increases the risk of disease and may worsen eye problems. The disorder results from an antibody, called thyroid-stimulating immunoglobulin (TSI) that has a similar effect to thyroid stimulating hormone (TSH). These TSI antibodies cause the thyroid gland to produce excess thyroid hormone. The diagnosis may be suspected based on symptoms and confirmed with blood tests and radioiodine uptake. Typically, blood

tests show a raised T3 and T4, low TSH, increased radioiodine uptake in all areas of the thyroid, and TSI antibodies. The three treatment options are radioiodine therapy, medications, and thyroid surgery. Radioiodine therapy involves taking iodine-131 by mouth, which is then concentrated in the thyroid and destroys it over weeks to months.[4] The resulting hypothyroidism is treated with synthetic thyroid hormone. Medications such as beta blockers may control some of the symptoms, and antithyroid medications such as methimazole may temporarily help people while other treatments are having effect. Surgery to remove the thyroid is another option. Eye problems may require additional treatments. Graves' disease will develop in about 0.5% of males and 3% of females. It occurs about 7.5 times more often in women than in men. Often, it starts between the ages of 40 and 60, but can begin at any age.[5] It is the most common cause of hyperthyroidism in the United States (about 50 to 80% of cases). The condition is named after Robert Graves, who described it in 1835. The exact cause is unclear; however, it is believed to involve a combination of genetic and environmental factors. While a theoretical mechanism occurs by which stress could cause an aggravation of the autoimmune response that leads to Graves' disease, more robust clinical data are needed for a firm conclusion. Thyroidectomy is considered as a prompt therapy for Grave's disease but it has few disadvantages such as scar post operatively, need for hospitalization, operation complications, recurrent laryngeal nerve, hypoparathyroidism, and intra-operative bleeding. This study evaluates all the factors that cause intra-operative blood loss and how it affects the grave's disease.

METHODS

This study was conducted on 200 patients with Grave's disease, who underwent thyroidectomy during the period from May 2010 to April 2016. The excluded patients were those who had undergone neck surgery before. For a period of 14 days, all patients were administered with potassium iodide before the surgery. Conventional open surgery or neck surgery video assisted were performed. Closed suction drainage tubes before wound closure in all patients were given and removed them 1 to 3 days later. If voice change was observed, recurrent laryngeal nerve injury was recorded. Those patients who had symptomatic hypocalcemia were given calcium supplements and vitamin D analogue. Variables of Clinical were measured. Students test and regression analysis was used to compare between groups. A p value of less than 0.05 was said to be statistically significant. For multivariate analysis, p value of ≤0.10 was considered to be stepwise regression analysis to determine the risk factors for intra-operative bleeding.

RESULTS

The majority of patients were females which constitute about 76.3% with a median age of 33 years. The median period between the onset of the disease and operation was 15 months. Weight of thyroid in grams was 40. Post-operative hospital stay was 4 hours.

Table 1: Demographics of patients in the study and operative variables.

Demographics of patients	
Age in years	33 (10-73)
Sex (male:female)	50:150
Period between disease onset and surgery	15 (1-460)

Table 2: Background of patients in the study and operative variables.

Indication for surgery	N (%)
Intolerance to antithyroid drug	80 (40)
Patient preference	45 (22.5)
Uncontrollable disease	45 (22.5)
Large goiter with pressure symptoms	40 (20)
Poor adherence	15 (7.5)
Grave's ophthalmology	10 (5)
Planned pregnancy	5 (2.5)
Malignancy suspicion	1 (0.5)
Thyrotoxic crisis	1 (0.5)
Young age	1 (0.5)
Failure of radioiodine therapy	1 (0.5)
Pre-operative TSH at initial consultation (ng/ml)	0.004 (0.0-77.5)
Pre-operative free T4 at initial consultation (ng/ml)	2.5 (0.2-21.2)
Pre-operative steroid	35 (17.5)
Pre-operative β-blocker	80 (40)

Table 3: Variables of the surgery.

Variables of surgery	N (range)
Duration of surgery (mins)	185 (68-378)
Amount of blood loss (ml)	95 (10-1385)
Blood transfusion	5

Table 4: Operative methods and surgical complications.

Variable	Values
Operative methods	
Open surgery:video assisted neck surgery	120:70
Subtotal: near total/total thyroidectomy	135:55
Surgical complications	**N (%)**
Transient hypocalcemia	38 (19)
Permanent hypoparathyroidism	1 (0.5)
Transient recurrent laryngeal nerve palsy	5 (2.5)
Permanent recurrent laryngeal nerve palsy	0 (0.0)

Table 5: Correlation between clinical variables and intra-operative blood loss (univariate analysis).

Variable	Correlation coefficient	P value
Continuous variables (regression analysis)		
Age in years	0.07	0.25
BMI	0.04	0.45
Period between disease onset and surgery	0.34	<0.001
Free T4 at initial consultation	0.20	<0.05
Weight of thyroid	0.70	<0.0001
Categorical variables (students t test)		
Sex		0.50
Operative methods		0.10
Type of surgical resection		0.50

DISCUSSION

Yamanouchi et al reported that a total of 197 patients underwent thyroidectomy for Graves' disease between 2002 and 2012.[6] It was evaluated that clinical factors that would be potentially related to AIOBL retrospectively. 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 be- tween 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 autotransfusion, 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. Grodski et al, conducted a study in which the most frequent absolute indication was the presence of a large goiter (n=8; 13%) or associated thyroid nodule (n=6; 10%).[7] Ophthalmopathy, a relative indication, comprised the largest single group overall (n=18; 29%); however, a significant number of patients (n=17; 27%) elected surgery in the absence of a recognized indication. There was strong concordance (73%) between the recorded indication and the patients' survey response. Overall, there was a high level of satisfaction with surgery with 88% of respondents giving a satisfaction score of 7 or greater on a visual analog scale (VAS) (0-10). Erbil et al reported that the mean blood flow, MVD, CD-34 expression, and blood loss in group 1 patients were significantly lower than those in group 2 patients.[8] There was a negative correlation between Lugol solution treatment and blood flow ($r(s)=-0.629$; $p=0.0001$), blood loss ($r(s)=-0.621$; $p=0.0001$), MVD ($r(s)=-0.865$; $p= 0.0001$), and CD-34 expression ($r(s)=-0.865$; $p=0.0001$). According to logistic regression analysis, Lugol solution treatment resulted in a 9.33 fold decreased rate of intraoperative blood loss. Karamanakos et al observed that a total, near-total and subtotal thyroidectomy was performed in 1,149,777 and 117 patients, respectively.[9] Transient RLNP occurred in 34 (1.6%) and permanent in 19 (0.9%) patients. Multivariate logistic regression analysis showed that extended resection (OR-odds ratio-1.6), Graves' disease (OR 2.7), thyroiditis (OR 2.1), recurrent goiter (OR 2.3) and thyroid malignancy (OR 1.7) were all independent risk factors for transient RLNP, whereas Graves' disease (OR 2.2) and recurrent goiter (OR 1.7) emerged as independent risk factors for permanent RLNP. The rates of transient and permanent hypopara-thyroidism were 27.8% and 4.8%, respectively. Multivariate analysis for transient hypoparathyroidism revealed that the extent of surgical resection (OR 2.2), Graves' disease (OR 2.1), recurrent goiter (OR 1.7), female gender (OR 1.5) and specimen weight (OR 1.6) were independent predictors. However, the extent of surgical resection (OR 2.7), Graves' disease (OR 1.8), recurrent goiter (OR 1.5) and malignant disease (OR 1.5) were independent risk factors for permanent hypoparathyroidism. Postoperative wound infection and hematoma occurred in 6 (0.3%) and 27 (1.3%) patients, respectively. No correlation was observed between wound infection or postoperative hemorrhage and the extent of surgery. Allannic et al performed a prospective randomized study was performed in patients with hyperthyroid Graves' disease (GD) in order to compare long (18 months) and short term (6 months) antithyroid drug treatment on the remission rate.[10] A therapeutic protocol was offered to all GD patients who had not been treated for this disease previously. All patients studied who followed the protocol were rechecked 2 year after treatment was withdrawn, or earlier in the case of relapse. Of the patients having undergone long term treatment, 61.8% still were in remission 2 year after treatment withdrawal, whereas only 41.7% of the patients treated for 6 months were in remission (P less than 0.05). Such findings clearly establish that treatment duration has a direct beneficial incidence on the remission rate. These results were confirmed by the fact that treatment for 18 months resulted in remission in 7 of 15 patients who had previously relapsed after a 6-month course of therapy. This improvement in relation to treatment duration might be due to the immunosuppressive action of carbimazole. No significant difference was observed between relapse and remission groups, regardless of treatment duration,

for HLA ABDr, serum T3 and T4, and T3/T4 ratio determined before treatment. Only the thyroid-stimulating antibody levels determined at the time of diagnosis and at the end of treatment were higher in the relapse group, a difference that was relevant only globally, due to value scattering.

CONCLUSION

For Grave's disease, for excessive bleeding during surgery, a large goiter presented as a predictive factor, and transfusion of blood should be considered in cases in which goiter weighs more than 200 g.

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