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Surgical Management of Graves' Hyperthyroidism in Saudi Arabia: A Retrospective Hospital Study

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The aim of the study was to determine surgical indication and complication of subtotal thyroidectomy in patients being treated for Graves' disease at King Khalid University Hospital Riyadh Saudi Arabia in the period between January 1996 and December 2005. Twenty-five out of 194 adult patients with Graves' disease had thyroidectomy for hyperthyroidism during the 10-year period representing 13% comprising 11 males and 14 females. Mean age at presentation for all the patients was 28±12 years. Males had higher serum T₄ 77.7±20.7 than females 49.8±21.9 pmol L⁻¹; p<0.05. Serum T₃ levels were similar in both groups 31.9±15.2 for males and 29.4±15.7 pmol L⁻¹ for females, p = NS. Failure of antithyroid and/or radioiodine along with severe ophthalmopathy (52%), patient preference (12%) and large goiter alone (8%) were major indications for thyroidectomy in this group. Permanent remission occurred in 15 patients (60%) following the surgery. Hypothyroidism and relapse were observed in 16 (64%) and 4 (16%) of patients, respectively. One patient (4%) each experienced permanent recurrent laryngeal nerve palsy and hypoparathyroidism. It was concluded that more males than females with severe hyperthyroidism had thyroidectomy and that failure of antithyroid/radioiodine treatment and severe ophthalmopathy were the commonest indications for surgery in patients in patients with Graves' disease while post surgical permanent hypoparathyroidism and recurrent laryngeal nerve palsy were uncommon.

Key words: Graves' disease, thyroidectomy, treatment

INTRODUCTION

Surgical management of Graves' disease has been a successful modality in treating patients with hyperthyroidism worldwide with variable indications and post surgical course (Tschantz *et al.*, 2001; Pradeep *et al.*, 2007). Yet data from the central region of Saudi Arabia is lacking. As far as we know no detailed report available addressing local experience which will be used in guiding physicians and endocrinologists in pre- and post-surgical care of patients with Graves' disease. Furthermore, with fewer thyroidectomies for Graves' disease means such studies are valuable to surgeons and physicians in understanding anticipated outcome of the surgical procedure. The aims of the study were to determine indications and complications of thyroidectomies for adult patients with Graves' disease at our center.

MATERIALS AND METHODS

We conducted a retrospective chart review of 194 consecutive patients who presented or referred with Graves' disease to the endocrine clinic at King Khalid University Hospital (KKUH), Riyadh, Saudi Arabia between January 1996 and December 2005 following approval from the ethics committee. Graves' disease was defined as the presence of biochemical hyperthyroidism (elevated serum free T₄ concentration and undetectable TSH) together with an elevated diffuse thyroid uptake seen in ^{99m}Tc-pertechnetate scan. If an uptake scan was not available, the presence of biochemical hyperthyroidism with two of the following was required: diffuse goiter, significant titer of thyroid peroxidase and/or thyroglobulin autoantibodies (a titer of 1:100 was considered significant) and presence of thyroid ophthalmopathy. Data were also collected from archived laboratory data and when needed, from discussion with the patients endocrinologist. Free T₄, Free T₃ and TSH were measured by ELISA (Enzymun-Test, Boehringer Mannheim Immunodiagnosics, Mannheim, Germany) until year 2000 and then by electrochemiluminescence immunoassay (Roche Diagnostics, Indianapolis, IN, USA). Thyroid autoantibodies were measured by an antibody agglutination test (SERODIA-AMC and SERODIA-ATG, FUJIREBIO INC., Tokyo, Japan). The presence or absence of goiter was assessed clinically by a staff endocrinologist during the patient first visit to the endocrine clinic. The size of goiter could not be retrieved due to lack of documentation. Eye disease was defined according to the presence of eye signs in categories 2-6 of

the NOSPECS classification (Werner, 1977). All patients referred for surgery had subtotal thyroidectomy with thyroid tissue remnant 6-8 g. The following factors were assessed and recorded in the database for patients who underwent thyroidectomies: gender, age at diagnosis, indication for surgery, immediate and long-term post-operative complications, autoantibody status and titer and serum concentration of TSH, free T₄ and free T₃ at the time of initial assessment at diagnosis.

RESULTS

Of the 194 patients with Graves' hyperthyroidism seen in the 20 year period, 25 patients representing 13% of which 11 were males (ratio 1:1.3). Mean age at presentation was 28±12 years. Males had higher serum T₄ 77.7±20.7 than females 49.8±21.9 pmol L⁻¹; p<0.05. Serum T₃ levels were similar in both groups 31.9±15.2 for males and 29.4±15.7 pmol L⁻¹ for females, p = NS. Mean follow-up for the patients was 44.5±33.0 months.

Table 1 shows indications of surgery in the study group. Failed medical and/or radioiodine therapy along with presence of severe ophthalmopathy accounted for 52% of patients with Graves' hyperthyroidism, followed by failed antithyroid drugs and/or radiotherapy alone in 3 subjects (12%). Patient preference contributed 12% of patients subjected to thyroidectomy. On the other hand, two-third of patients had hypothyroidism following thyroid surgery for hyperthyroidism and 3 patients (12%) had relapse and resumed medical therapy after the surgery as depicted in Table 2.

Fifteen patients (60%) had an un-eventful surgical course. Three patients (12%) experienced prolonged hypocalcemia beyond one week while one patient each (4%) had permanent hypoparathyroidism and recurrent laryngeal nerve palsy, respectively (Table 3).

Table 1: Indications of surgery in twenty-four patients with Graves' disease

Parameters	No. (%)
Failed antithyroid/RAI±severe ophthalmopathy	13 (52)
Failed antithyroid/RAI therapy	3 (12)
Patient preference	3 (12)
Large goiter	2 (8)
Failed antithyroid/RAI±large goiter	2 (8)
Failed antithyroid/RAI±severe ophthalmopathy±large goiter	1 (4)
Antithyroid drugs not available	1 (4)

Table 2: Outcome of surgery in twenty-five patients with Graves' disease

Parameters	No. (%)
Hypothyroidism	16 (64)
Still being followed-up	4 (16)
Needed antithyroid agent	3 (12)
Needed radioiodine therapy	1 (4)
Lost to follow up	1 (4)

Table 3: Complications of surgery in twenty-five patients with Graves' disease

Parameters	No. (%)
No complications	15 (60)
Still being followed-up	4 (16)
Hypocalcemia beyond 7 days	3 (12)
Permanent recurrent laryngeal nerve palsy	1 (4)
Permanent hypocalcemia	1 (4)
Lost to follow up	1 (4)

DISCUSSION

We have shown that the principal indication for surgical management of Graves' hyperthyroidism to be failure of initial medico-radioiodine therapy with or without severe eye disease, similar to recent observation by others (van Isselt and van Dongen, 2004; Scharf *et al.*, 2006). Although present study population is relatively small, it reflected the change in the approach to management of the disease over the years. In early sixties, surgery and antithyroid agents were the first treatment of choice for Graves' disease (Streetman and Khanderia, 2003). However, with the proven safety of radioiodine, the latter has currently assumed first line therapy worldwide (Weber *et al.*, 2006). The declining role of surgery in management of hyperthyroidism in our environment clearly shown in this study where we recorded 12% as against 25% reported in the region one and a half decades ago (Sulimani *et al.*, 1989). Similarly, we observed low rate of patient preference as indication for the surgery. For instance Lal *et al.* (2005) and Grodski *et al.* (2007) reported 27% patient preference for thyroidectomy in contrast to 12% in present study. The reason for this is not clear although public education on safety of radioiodine as well as its availability at our center might be responsible (Ghadban *et al.*, 2003).

Another interesting finding of present study was the role of severe ophthalmopathy as an indication for surgery. It was shown from our data that 52% of patients had thyroidectomy after trial but failed radioiodine or antithyroid agents. It showed despite the reported worsening of eye symptoms following radioiodine therapy, surgery still being considered as a second line therapy. Indeed none of the patients with severe eye disease had surgery without initial medical or radioiodine therapy. Palestini *et al.* (2005) reported 23% of patients with Graves' disease had thyroidectomy due to severe eye disease. However all our subjects with severe ophthalmopathy were referred for surgery in the presence of an added indication such as failed medical/radiotherapy or large goiter.

Hypothyroidism was found to be the commonest outcome following thyroidectomy in our study population similar to others report but sharply differed from others findings in which less than 10% were reported

(Moreno *et al.*, 2006). It showed hypothyroidism to be an expected outcome and thus not be regarded as complication of the surgery. On the other hand 16% of the patients had relapse after thyroidectomy similar to others reports (Moreno *et al.*, 2006) but higher than recent reports in the literature in which less than 5% relapse was achieved (Ben Gamra *et al.*, 2004; Okamoto *et al.*, 1992). The relative greater percentage of post surgical relapse might be due to smaller number of subjects. However, Kostka *et al.* (2004) reported experienced surgeon to be the determinant factor to achieving higher surgical success rate. In present study of 10 year period involving 25 patients more than 10 surgeons (data not shown) operated and thus might explain the higher percentage of relapse recorded due possibly to limited exposure. Moreno *et al.* (2006) in a related review reported remnant thyroid tissue to be the main factor to achieving remission after thyroidectomy. However, it is important to note that there is a limitation to retrospective studies in general. Observations derived from such studies may contain some missing information and thus may serve as a stimulus to further prospective work to clarify findings. The present study must be interpreted in the knowledge of the defects inherent in such studies. Nevertheless, present result is in agreement with other reports (Bhansali and Chandalia, 2002; Schussler-Fiorenza *et al.*, 2006; Werga-Kiellman *et al.*, 2001).

The most serious complications in present study were recurrent laryngeal nerve palsy and permanent hypoparathyroidism each contributing 4%. Ben Gamra *et al.* (2004) reported these complications to be less than 1% in a larger retrospective study. Similarly, in a landmark 10 year review, Werga-Kiellman *et al.* (2001) recorded post surgical permanent hypoparathyroidism at 1%. A closer look at our data however showed only one patient each experienced permanent hypocalcemia and recurrent laryngeal nerve palsy further supporting rarity of the two surgical complications in management of Graves' hyperthyroidism.

Interestingly, present study revealed a relative over representation of males who had thyroid surgery in contrast to consistent findings of female dominance in most reports (Agarwal and Mishra, 2001; Diez, 2003). Although Graves' disease being a predominantly female disease with a ratio of 1:5, we found 48% of males had thyroidectomy for Graves' hyperthyroidism. The reason for this is not obvious. However, serum T₄ levels were shown to be significantly higher in males than females indicating the former to have more severe disease and might be an indication for surgery with initial failure to other treatment modalities. In view of these, further studies on a larger population are however needed to characterize present findings.

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