

RECURRENT NODULAR GOITER PREDICTORS OF RECURRENCE AND OUTCOME AFTER REOPERATION

Mohamed Rabea, MD and, Mohamed Al-Ahmer, MD

*Department of General Surgery, Faculty of Medicine, EL-Minia University.
Department of Otorhinolaryngology, Faculty of Medicine, AL-Azhar University

Keywords:

Goiter- Thyroidectomy -
Recurrence.

Abstract

Objective: To determine the predictors of recurrent nodular goiter and the incidence of complications related to reoperation.

Patients and Methods: The study included 25 patients underwent reoperative thyroid surgery for management of recurrent nodular goiter. A matched case-control study of 25 patients operated on for non recurrent nodular goiter at the same period was performed. The assessed parameters include: age and sex, indication for primary and reoperative surgery, interval between primary and reoperative surgery, pathologic findings, duration of reoperative surgery, duration of hospital stay, and postoperative complications. The standard operation for strictly unilateral thyroid disease was hemithyroidectomy with resection of the isthmus. A total thyroidectomy was performed in cases of cancer or when nodules were present in both thyroid lobes.

Results: The study included 25 patients with recurrent goiter (10 male and 15 female) with mean age of 43 ± 12.2 years. The mean interval between primary and reoperative thyroidectomy was 12 ± 3.5 years. The indication for reoperation was mostly due to an originally misdiagnosed carcinoma (68%). Papillary carcinoma was the most common histopathological type (40%). Age younger than 40 years, presence of multinodular goiter at initial surgery and bilateral surgery were significantly frequent risk factors in patients with recurrent goiter, while multinodular goiter was the only significant independent predictor of the recurrence. Total thyroidectomy was the most frequently performed secondary procedure (84%). The morbidity rate was 16% in patients with reoperative thyroidectomy (temporary hypoparathyroidism in 12% and temporary RLN palsy in 4%). The rate of temporary hypoparathyroidism was 4% in patients with first time thyroidectomy.

Conclusion: Presence of multinodular goiter at primary surgery is a predictor of recurrent goiter, thus total thyroidectomy is advisable in these cases which can be done safely as a primary or a secondary procedure with an acceptable rate of complications when standard technical considerations were respected.

Introduction

The recurrent goiter is the regrowth of thyroid tissue after thyroidectomy. An inadequate surgical removal of the thyroid gland, lack of substitution therapy and pathological stimulation of the thyroid growth can all promote the recurrence [1]. The rate of recurrence after partial resection of the thyroid gland in the literature varies between 2.2% and 49% [2-4].

Operation for recurrent goiter is sometimes indicated for nodular recurrence after partial surgery for initially benign thyroid disease or for a completion total thyroidectomy when a final diagnosis of well-differentiated thyroid cancer has been achieved. However, this surgery can expose the patient to postoperative complications such as recurrent laryngeal nerve (RLN) palsy or hypoparathyroidism [5, 6].

The purpose of this study was to identify the characteristics of recurrent nodular goiter, predictors of recurrence, treatment of choice and the incidence of complications related to reoperation.

Patients and Methods

The study included 25 patients (10 male and 15 female), who underwent reoperative thyroid surgery for management of recurrent nodular goiter at departments of General Surgery and ENT, Al- Jafel International Hospital, Riyadh, KSA between October 2009 and July 2013. The assessed clinical parameters include: patient age and sex, indication for primary and reoperative surgery, interval between primary and reoperative surgery, pathologic findings, duration of reoperative surgery, duration of hospital stay, and complications. Needle biopsy was done for all these cases preoperatively. To compare postoperative complications of initial and reoperative thyroidectomy and to identify the risk factors of recurrent goiter, a matched case-control study of 25 patients operated on for non recurrent nodular goiter at the same period was performed (9 male and 16 female). The standard operation for strictly unilateral thyroid disease was hemithyroidectomy (total lobectomy on one side) including resection of the isthmus. A total thyroidectomy was performed in cases of cancer or when nodules were present in both thyroid lobes. The secondary thyroidectomy was performed as previously described [7].

Dissection was started laterally by dividing the infrahyoid muscles to avoid the fibrous tissue around the thyroid remnant when the lobe had been partially removed during previous surgery. If the lobe to be resected had not been disturbed at prior operation, we went through the infrahyoid muscles to avoid fibrosis around the anterior face of the trachea. The first step was ligation of the superior thyroid vessels with special attention being paid to the superior parathyroid gland and the external branch of the superior laryngeal nerve. Then, the RLN was clearly identified in the lower part of the neck and traced very carefully along its cervical course. The inferior parathyroid gland was preserved when it was located far from the thyroid lobe. Any parathyroid gland that could not be salvaged because of its anatomic location was minced and placed in a sternocleidomastoid muscle. Intra-thoracic goiters extending into the superior mediastinum were removed by progressive traction through the collar incision. In cases with reoperation from thyroid cancer, lymph node metastasis diagnosed before or during surgery had a modified radical neck dissection, including resection of lymph nodes of the central compartment around the trachea (compartment VI) and those around the jugular vein extending from the carotid sheath to the trapezoid muscle and from the subclavian vein to the hypoglossal nerve (compartments II and IV) [8] (Shown in Fig. 1.)

Removed tissue was submitted for histopathological analyses in all cases (Shown in Fig. 2 & 3). All patients underwent routine preoperative and postoperative indirect laryngoscopy as well as postoperative measurement of calcium and parathyroid hormone levels. Temporary hypoparathyroidism was defined as symptomatic postoperative hypocalcemia while permanent hypoparathyroidism was defined by the requirement for ongoing calcium and vitamin D supplementation to avoid hypocalcaemia 12 months after surgery. Permanent RLN palsy was defined as the absence of vocal cord function 12 months after surgery.



Fig. 1 Multiple Recurrent nodules of the Left Lobe, Intraoperative

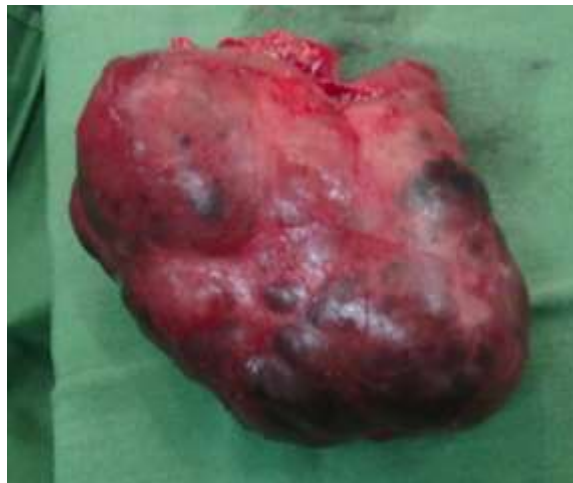


Fig.2 Bilateral Recurrent Benign Nodules



Fig. 3 Recurrent Malignant nodule of the Right Lobe

Statistical analysis:

The statistical analysis was done using Statistical Package for Social Sciences (SPSS) software (version 16, SPSS, Inc, Chicago, IL, USA). Continuous and categorical variables were displayed as means \pm standard deviation (SD) and percentages, respectively. Differences between categorical variables were analyzed by chi-square test or Fisher's exact test. The odds ratio (OR) and its 95% confidence interval (CI) were used to determine whether a particular exposure is a risk factor for recurrence of goiter. The significant factors on bivariate analysis entered multivariate analysis with stepwise linear regression to determine the independent predictors of recurrence after primary thyroidectomy. Statistical significance was set at $P < 0.05$.

Results

The characteristics of the studied 25 patients with recurrent goiter underwent reoperative thyroidectomy are shown in (Table 1). There were 10 (40%) male and 15 (60%) female patients who had mean age of 43 ± 12.2 years (range 20 to 70 years). The type of goiter in the group of reoperative thyroidectomy was multinodular in 19 patients (76%) and uninodular in 6 patients (24%). The disease was bilateral in 17 patients (68%) and unilateral in 8 patients (32%). The family history of goiter was present in 5 patients (20%). The interval between the primary and reoperative thyroidectomy ranged from 1 to 18 years with mean interval of 12 ± 3.5 years.

The indications for reoperation include: thyroid cancer in the resected specimen of relapsed or originally misdiagnosed carcinoma in 17 patients (68%) and recurrent benign thyroid disease in 8 patients (32%). Histopathological examination of the recurrent thyroid lesions before reoperation (Table 2) revealed: papillary carcinoma in 10 patients (40%), follicular carcinoma in 4 patients (16%), medullary carcinoma in 2 patients (8%), Hürthle cell carcinoma in one patient (4%) and benign lesions in 8 patients (32%).

The bivariate analysis of the risk factors in patients with reoperation and those with no reoperation (Table 3) revealed that age younger than 40 years, presence of multinodular goiter at initial surgery and bilateral surgery were a significantly frequent risk factors in patients with recurrent goiter ($P < 0.05$), with high odds ratio. On multivariate analysis of these significant risk factors using stepwise regression (Table 4), presence of multinodular goiter was a significant independent predictor of the recurrence after first thyroidectomy ($P < 0.05$).

In patients with reoperative thyroidectomy, the primary procedures include: subtotal thyroidectomy in 14 patients (56%), hemithyroidectomy in 7 patients (28%) and total thyroidectomy in 4 patients (16%), while the secondary procedures include: total thyroidectomy in 21 patients (84%) and subtotal thyroidectomy in 4 patients (16%). The duration for reoperation surgery was 120 ± 35 minutes. The duration of postoperative hospital stay was 7 ± 3 days. Post-operative complications (Table 5) were discovered in 4 patients (16%); 3 patients (12%) with temporary hypoparathyroidism and one patient (4%) with temporary recurrent laryngeal nerve (RLN) palsy related to reoperative thyroidectomy. In the control group (no reoperation), there was one patient (4%) had postoperative complication related to the surgical procedure in the form of temporary hypoparathyroidism.

Table (1): Characteristics of 25 patients with recurrent goiter

Characteristics	Recurrent goiter (N=25)
Age (years)	43 ± 12.2
Sex:	
Female	15(60%)
Male	10(40%)
Type of goiter:	
Multinodular	19(76%)
Uninodular	6(24%)
Side of goiter:	
Bilateral	17(68%)
Unilateral	8(32%)
Family history of goiter	5(20%)
Interval to reoperation (years)	12 ± 3.5

Table (2): Histopathological examination of the recurrent thyroid lesions before reoperation

Histopathological findings	Recurrent goiter (N=25)
Malignant lesions:	17(68%)
Papillary carcinoma	10(40%)
Follicular carcinoma	4(16%)
medullary carcinoma	2(8%)
Hürthle cell carcinoma	1(4%)
Benign lesions	8(32%)

Table (3): Bivariate analysis of the risk factors for recurrent goiter

Risk factors	Reoperation	No reoperation	P-value	Odds ratio (95%CI)
Age:				
<40 years	19(76%)	12(48%)	0.04*	3.4(1.02-11.47)
>40 years	6(24%)	13(52%)		
Sex:				
Female	15(60%)	16(64%)	0.77	0.84(0.26-2.64)
Male	10(40%)	9(36%)		
Family history:				
Present	5(20%)	1(4%)	0.08	6(0.64 to 55.6)
Absent	20(80%)	24(96%)		
Type of goiter:				
Multinodular	19(76%)	11(44%)	0.02*	4(1.20-13.5)
Uninodular	6(24%)	14(56%)		
Side of goiter:				
Bilateral	17(68%)	9(36%)	0.02*	3.7(1.17-12.1)
Unilateral	8(32%)	16(64%)		

*significant difference

Table (4): Multivariate analysis of the risk factors for recurrent nodular goiter

Variables	Beta	t-value	P-value
Multinodular goiter	0.32	2.39	0.02*
Age <40 years	-0.30	-0.63	0.52
Bilateral goiter	0.15	0.59	0.55

*significant predictor

Table (5): Post-operative complications in patients with reoperative thyroidectomy and those with no reoperation

Complications	Reoperation	No reoperation	P-value
Total number	4(16%)	1(4%)	0.15
Temporary hypoparathyroidism	3(12%)	1(4%)	0.29
Temporary recurrent laryngeal nerve palsy	1(4%)	0(0%)	0.31

Discussion

Nodular goiter encompasses a spectrum of diseases from the incidental asymptomatic small solitary nodule to the large goiter causing pressure symptoms as well as functional complaints [9]. The total and subtotal thyroidectomy are major surgical methods for treatment of nodular goiter and subtotal thyroidectomy is the standard method [10]. Studies in literature revealed that the recurrence rate of nodular goiter ranged between 3-50% after surgery [11-13]. In the present study, age younger than 40 years, presence of multinodular goiter at initial surgery and bilateral surgery were significantly frequent risk factors in patients with recurrent goiter, while multinodular goiter was the only significant independent predictor of the recurrence after first thyroidectomy. Therefore, we can state that

complete removal of all detectable nodules and total thyroidectomy for multinodular goiter may be helpful to reduce the recurrence rate in this instance. In literature, there is a controversy regarding the clinical criteria for the risk of recurrence of nodular goiter. The study by Gibelin et al [5] showed that the age of <40 years and multiple nodules are the risk factors of recurrence after subtotal thyroidectomy, and it could be recommended that total thyroidectomy for patients with bilateral multinodular goiter is preferred aiming to prevent a second surgery due to recurrence.

In the study by Ríos-Zambudio et al [14], risk factors detected in the multivariate study were youngest age, surgeon's lack of experience in endocrine surgery, and the surgical technique. Thus, it was implicated that partial resection techniques should be carried out by surgeons with experience and there should be avoided in young patients. In the present study, the interval between the primary and reoperative thyroidectomy ranged from 1 to 18 years with mean interval of 12 ± 3.5 years. In literature, most of the recurrences developed 10 to 20 years after the previous surgery [15], although some authors recommend 30 years of follow-up to determine the actual outcome [16-18]. In the present study, the most frequent primary procedure in patients with reoperative thyroidectomy was subtotal thyroidectomy (56%). In literature, despite routine use of postoperative levothyroxine therapy recurrence may occur after subtotal thyroidectomy. The incidence of recurrence has been directly related to a long postoperative follow-up period and to large amounts of remnant tissue [19, 20]. The study by Delbridge et al [21] showed that subtotal thyroidectomy in multinodular goiter has resulted in reoperation for recurrence in 13% to 20% of patients, reaching a peak incidence 13 years after the primary operation.

The performance of total thyroidectomy in multinodular disease has been reserved for exceptionally large goiters. Opponents of total thyroidectomy claim that the procedure is not justified in multinodular disease, as the risk for malignancy is low but associated complication rates are high [22]. The study by Bononi et al [23] regards total thyroidectomy as the most effective method to prevent recurrences. When it is performed by an experienced surgeon the rate of complications is not higher in comparison to subtotal thyroidectomy and especially to excision of recurrent goiter. In the present study, the rate of temporary RLN palsy was 4% with no cases of permanent RLN palsy. In literature, the incidence of temporary and permanent palsy of recurrent laryngeal nerve may be as high as 20% in recurrent goiters [24]. In literature, reoperative thyroid surgery had more frequent recurrent laryngeal nerve injuries, both temporary (0-22%) and permanent (0-13%) [7]. The most likely causes of temporary nerve damage are excessive mobilization during surgery, axonal damage due to excessive scar tissue, thermal lacerations during cauterization, and difficult intubation [25].

In the present study, the rate of temporary hypoparathyroidism was 12% with no cases of permanent hypoparathyroidism. In literature, a higher risk of hypoparathyroidism was noticed in reoperative thyroid surgery. It has been reported that the incidence of transient hypoparathyroidism was 0% to 25% and of definitive hypoparathyroidism from 0% to 22% [26, 27]. Hypocalcemia after thyroidectomy might be caused by direct trauma to the parathyroid glands, their incidental removal, and ischemia. Fortunately, most cases of hypocalcemia after thyroidectomy are temporary. The severity and duration of hypocalcemia are thought to be directly related to the extent of dissection during thyroidectomy [28].

In conclusion, reoperative thyroid surgery results in a high rate of postoperative complications but it can be done safely with little complications in an experienced hands. The presence of multinodular goiter at the initial operation carries a significant risk of recurrence. To minimize the potential of a reoperation, specific rules of surgical techniques should be emphasized and removal of all nodules or total thyroidectomy by experienced endocrine surgeons is advisable.

References

1. Rudnicki J, Agrawal AK, Jelen M, Sebastian M, Sroczynski M, Zysko D. Histopathological evaluation of recurrent goiter. *Folia Histochem Cytobiol.* 2010;48(3):430-3.
2. Moley JF, Lairmore TC, Doherty GM, et al. Preservation of the recurrent laryngeal nerves in thyroid and parathyroid reoperations. *Surg.* 1999;126(4):673-7.
3. Basili G, Biagini C, Manetti A, et al. Risk of recurrence following partial thyroidectomy for benign lesions. Report of 58 patients 15-25 years after surgery. *Minerva Chir.* 2003;58(3):321-9.

4. Cappellani A, Di Vita M, Zanghì A, Lo Menzo E, Cavallaro A, Alfano G, Giuffrida D. The recurrent goiter: prevention and management. *Ann Ital Chir.* 2008;79(4):247-53.
5. Gibelin H, Sierra M, Mothes D, Ingrand P, Levillain P, Jones C, Hadjadj S, Torremocha F, Marechaud R, Barbier J, Kraimps JL. Risk factors for recurrent nodular goiter after thyroidectomy for benign disease: case-control study of 244 patients. *World J Surg.* 2004;28(11):1079-82.
6. Lefevre JH, Tresallet C, Leenhardt L, Jublanc C, Chigot JP, Menegaux F. Reoperative surgery for thyroid disease. *Langenbecks Arch Surg.* 2007;392(6):685-91.
7. Menegaux F, Turpin G, Dahman M, Leenhardt L, Chadarevian R, Aurengo A, Du Pasquier L, Chigot JP. Secondary thyroidectomy in patients with prior thyroid surgery for benign disease: A study of 203 cases. *Surg.* 1999; 125:479-483.
8. Cooper DS, Doherty GM, Haugen BR, Kloos RT, Lee SL, Mandel SJ, Mazzaferri EL, McIver B, Sherman SI, Tuttle RM. Management guidelines for patients with thyroid nodules and differentiated thyroid cancer (The American Thyroid Association Guidelines Taskforce). *Thyroid.* 2006; 16(2):1-34.
9. Pelizzo MR, Merante Boschin I, Toniato A, Sorgato N, Marzola MC, Rubello D. Surgical therapeutic planning options in nodular goiter. *Minerva Endocrinol.* 2010;35(3):173-85.
10. Unalp HR, Erbil Y, Akguner T, Kamer E, Derici H, Issever H. Does near total thyroidectomy offer advantage over total thyroidectomy in terms of postoperative hypocalcemia? *Int J Surg.* 2009; 7(2):120-5.
11. Colak T, Akca T, Kanik A, Yapici D, Aydin S. Total versus subtotal thyroidectomy for the management of benign multinodular goiter in an endemic region. *ANZ J Surg.* 2004;74:974-8.
12. Terris DJ, Khichi S, Anderson SK, Seybt MW. Reoperative thyroidectomy for benign thyroid disease. *Head Neck.* 2010;32: 285-9.
13. Tezelman S, Borucu I, Senyurek Giles Y, Tunca F, Terzioglu T. The change in surgical practice from subtotal to near-total or total thyroidectomy in the treatment of patients with benign multinodular goiter. *World J Surg.* 2009; 33(3):400-5.
14. Rios-Zambudio A, Rodríguez-González JM, Galindo-Fernández PJ, Montoya-Tabares MJ, Canteras-Jordana M, Parrilla-Paricio P. Clinical recurrence of multinodular goiter after surgery. A multivariate study on the risk factors. *Rev Clin Esp.* 2005;205(1):9-13.
15. Giles Y, Boztepe H, Terzioglu T, Tezelman S. The advantage of total thyroidectomy to avoid reoperation for incidental thyroid cancer in multinodular goiter. 2004;139(2):179-82.
16. Visset J, Lumingu K, Le Bodic MF, Paineau J, Letessier E. Total thyroidectomy to prevent recurrence of benign thyroid goiter [in French]. *Chirurgie.* 1991;117: 37-40.
17. Kraimps JL, Marechaud R, Gineste D. Analysis and prevention of recurrent goiter. *Surg Gynecol Obstet.* 1993;176:319-322.
18. Delbridge L, Guinea AI, Reeve TS. Total thyroidectomy for bilateral benign multinodular goiter: effect of changing practice. *Arch Surg.* 1999;134:1389-1393.
19. Rojdmarm J, Jarhult J. High long term recurrence rate after subtotal thyroidectomy for nodular goitre. *Eur J Surg.* 1995;161:725-727.
20. Reeve TS, Delbridge L, Brady P, et al. Secondary thyroidectomy: a twenty-year experience. *World J Surg.* 1998;12:449-453.
21. Delbridge L, Guinea AI, Reeve TS. Total thyroidectomy for bilateral benign multinodular goiter: effect of changing practice. *Arch Surg.* 1999;134:1389-1393.
22. Foster RS Jr. Morbidity and mortality after thyroidectomy. *Surg Gynecol Obstet.* 1978;146:423-429.
23. Bononi M, de Cesare A, Atella F. Surgical treatment of multinodular goiter: incidence of lesions of the recurrent nerves after total thyroidectomy. *Int Surg.* 2000;85(3):190- 193.
24. Johnson S, Goldenberg D. Intraoperative Monitoring of the Recurrent Laryngeal Nerve During Revision Thyroid Surgery. *Otolaryngol Clin N Am.* 2008;41:1147-54.
25. Rosato L, Avenia N, Bernante P, De Palma M, Gulino G, Nasi PG. Complications of thyroid surgery: Analysis of a multicentric study on 14,934 patients operated in Italy over 5 years. *World J Surg* 2004;28:271-6.
26. Moalem J, Suh I, Duh QY. Treatment and Prevention of Recurrence of Multinodular Goiter: An Evidence-based Review of the Literature. *World J Surg* 2008;32:1301-12.
27. Calò PG, Farris S, Tatti A, Piga G, Mallocci A, Nicolosi A. Le urgenze in chirurgia tiroidea. Nostra esperienza. *Chir Ital.* 2006;58:323-9.

28. Dogan L, Karaman N, Yilmaz KB, Ozaslan C, Atalay C. Total thyroidectomy for the surgical treatment of multinodular goiter. Surg Today. 2011;41(3):323-7.