

# Clinical Complications, Incidental Neoplasms and Recurrence in Surgical Management of Multi Nodular Goiter

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## Abstract

**Objectives:** To assess the clinical complications, incidental neoplasms and recurrence in different protocols of surgical management of multinodular goiter.

**Methods:** Thyroid tissue samples of 200 patients who underwent total thyroidectomy, near total thyroidectomy and subtotal thyroidectomy for surgical management of multinodular goiter were designed our study. The surgical procedures were performed between January 2016 and December 2018 in general surgery department MUST University. Preoperative ultrasound-guided fine needle aspiration cytology and the postoperative surgical specimens were delivered to pathology lab at MUST University 6<sup>th</sup> of October city, Giza. Patients with thyroid neoplasms, thyroiditis, toxic and recurrent goiter were excluded from the study. Personal and demographic data were collected and analyzed. Postoperative clinical complications and incidental neoplasms were evaluated. All the patients were followed up over 1 year for expected clinical complications, recurrence of goiter and appearance of neoplasms.

**Conclusion:** A lifelong replacement morning tablet of thyroid hormones is much more accepted than reoperation for incidental cancer or recurrence of goiter. Total thyroidectomy is the recommended optimum surgical procedure for multinodular goiter.

**Results:** A total number of 200 patients underwent thyroidectomy for surgical management of multinodular goiter. Female patients were 160 (80%) and male patients were 40 (20%) with a female to male ratio 4:1. Age of the patients ranged from 32 to 55 years (median 42.65±7.32). Five governorates were represented in this study. The highest ratio (65%) was detected in Oases and Giza. There were 170 (85%) cases of total thyroidectomy and 30 (15%) cases of subtotal thyroidectomy. Permanent recurrent laryngeal nerve injury was observed in one (0.6 %) patient in total thyroidectomy while temporarily recurrent laryngeal nerve injury was observed in 4 (2.4%) patients. Temporarily recurrent laryngeal nerve injury was observed in one (3%) patient in subtotal thyroidectomy. Permanent hypocalcemia was observed in 2 (1%) patients in total thyroidectomy while temporarily hypocalcemia was observed in 10 patients (5.9%). Temporarily hypocalcemia was observed in one patient (3%) in subtotal thyroidectomy. Permanent hypothyroidism occurred in all patients in total thyroidectomy and 12 (40%) patients in subtotal thyroidectomy. Follicular adenoma was observed in 4 (2.4%) patients in total thyroidectomy and in 4 (13%) patients in subtotal thyroidectomy. Papillary carcinoma was observed in 5 (3%) patients in total thyroidectomy and 2 (6.7%) patients in subtotal thyroidectomy. During follow up period, recurrence of goiter was noted in 6 (20%) patients in subtotal thyroidectomy.

**Keywords:** Multinodular goiter; Complications; Incidental neoplasms; Recurrence

## Introduction

Goiter is the most common endocrine disorder requiring surgical intervention, especially in endemic areas. The World Health Organization (WHO) notified that 5% of the world's population experienced goiter and that 75% of these people live in iodine deficient areas [1]. In Egypt, endemic goiter and low urinary iodine concentration have been reported in several regions [2]. Multinodular goiter (MNG) includes a spectrum of clinical aspects, histologically formed of multiple hyperplastic follicles scattered in a nodular form throughout an enlarged thyroid gland [3]. Cosmetic problem, compressive symptoms, toxicity and suspicion of malignancy comprised the major indications for surgery [4]. Several surgical protocols were dealing with goiter such as subtotal thyroidectomy (STT), near total thyroidectomy (NTT) and total thyroidectomy (TT) [5]. The optimum surgical procedure for treatment of goiter was still under debate [6]. STT was selected for its lower rate of postoperative complications and unnecessary postoperative hormone replacement therapy. Nevertheless, STT has a high recurrence rate which causes reoperation morbidities and most of the patients need thyroxin therapy after surgery [5]. NTT was a less complicated surgical option that has been evolved as comprise between STT and TT [7]. The aim of surgeons performing STT or NTT for MNG was to try keeping the patients

euthyroid postoperatively and avoiding the need for lifelong thyroid hormone replacement. Despite the little remnants of thyroid tissue in these surgical procedures, the necessity of treatment with thyroid hormone was remained [8]. Regardless the lifelong needs of hormone replacement therapy, TT have become a frequently practiced surgical method over the last years [9]. Although TT was widely accepted for primary management of thyroid cancer [10], controversy continued to surround its routine use for the management of benign MNG [11]. TT can be practiced with low complication rates if the thyroid tissue was dissected carefully and the parathyroid glands and the recurrent laryngeal nerve were identified and protected [12]. Incidental thyroid cancer was a term applied to a very small, unsuspected cancer detected accidentally on pathologic examination of thyroid tissue removed for benign disease [13]. This study aimed to assess the clinical complications, incidental neoplasms and recurrence in different protocols of surgical management of MNG.

## Methods and Investigations

Thyroid tissue samples of 200 patients who underwent TT, NTT and STT for surgical management MNG were designed our prospective study. The surgical procedures were performed between January 2016 and December 2018. The patients were admitted to general surgery department at MUST University. The preoperative ultrasound-guided fine needle aspiration cytology (FNAC) and postoperative surgical specimens were delivered to pathology lab at MUST University 6<sup>th</sup> of October city, Giza, Egypt. Approval for this study was obtained from the Medical Ethics Committee of MUST University. Inclusion criteria comprised patients with MNG. Exclusion criteria included patients with thyroid neoplasms, thyroiditis, toxic and recurrent goiter. Personal and demographic data were collected. Postoperative clinical complications and incidental neoplasms were evaluated. All the patients were followed up over 1 year for expected clinical complications, recurrence of goiter and appearance of neoplasms.

### Surgical procedures

The surgical procedures of TT, NTT and STT were comprised a resection of variable amount of both thyroid lobes based on the gland and nodules status respecting the benign nature of MNG. The TT technique included complete excision of both thyroid lobes and isthmus sparing recurrent laryngeal nerve and parathyroid glands two in each side. The NTT technique constituted the excision of both lobes of the gland leaving a small cuff of thyroid gland. STT technique is like NTT but the remaining part of the gland is equivalent to normal thyroid lobes (8 grams) on each side. The indications for surgical management of MNG in 200 patients of this study were pressure symptoms (n=110), cosmetic problems (n= 70) and the presence of retrosternal goiter (n=20). In our practice TT took popularity (n=170) for MNG patients without healthy thyroid tissue in the postero-medial part of the gland. Much less number of patients underwent NTT (n=12) or STT (n=18) for management of MNG considering the presence of healthy postero-medial part of thyroid gland. The portion left was to provide hormonal requirements as well as to protect the recurrent laryngeal nerve and parathyroid glands.

### Clinical investigations

Preoperative ultrasound, free T3-T4, TSH levels and serum calcium concentration were assessed. Laryngoscopic examination of the vocal cords was performed in selected cases. All the included patients were rendered euthyroid before surgery.

Postoperative laryngoscopic examination of the vocal cords was carried out for all patients. During the follow-up period, patients with vocal cord movements turned to normal were regarded as having temporarily recurrent laryngeal nerve injury. When the injury lasted more than six months, it was regarded as permanent.

Serum calcium levels were determined on the first postoperative day and were estimated on the subsequent postoperative days as necessary. Patients with hypocalcemia symptoms were treated with vitamin D and calcium replacement. Patients with hypocalcemia symptoms lasting more than six months were considered as having permanent hypoparathyroidism.

All patients were discharged on L-thyroxin 100 µg daily as starting dose. During the follow up period, the proper dose of L-thyroxin was adjusted according to individual free T3-T4 and TSH levels. Permanent hypothyroidism was expected in all cases of TT. In NTT and STT the hypothyroidism was considered as being permanent when the hormone replacement therapy lasted for 6 months after surgery.

### Pathologic study

Preoperative ultrasound guided FNAC was performed for all patients of NTT and STT to confirm the clinical diagnosis of MNG and to exclude thyroid neoplasms. Twenty cases of TT underwent FNAC due to the presence of predominant nodules. Four slides for each patient were received, stained with H&E and the cytologic examination was conducted by the pathologist. Cases with FNAC diagnosis of colloid goiter were included in the study. Inflammatory, benign neoplastic and malignant results were excluded.

Postoperative surgical specimens were received at the pathology lab, fixed in 10% formalin, the paraffin blocks were cut in 4 µm sections with microtome and stained with H&E. All stained thyroid tissues were examined histologically under the light microscope and pathologic diagnosis was evaluated.

### Statistical analysis

Data were collected, revised, coded and entered to the Statistical Package for Social Science (IBM SPSS) version 23. The quantitative

data were presented as mean, standard deviations and ranges. Also qualitative variables were presented as number and percentages. The comparison between two groups with qualitative data was done by using Chi-square test and/or Fisher exact test only when the expected count was found less than 5 in any cell. The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value was considered significant at the level of  $< 0.05$ .

## Results

Our study included a total number of 200 patients who underwent TT, NTT and STT thyroidectomy for surgical treatment of MNG. According to the collected personal and demographic data (Table 1) 160 (80%) patients were females and 40 (20%) were males with a female to male ratio 4:1. The age of the patients was ranged from 32 to 55 years (median  $42.65 \pm 7.32$ ). Five governorates were represented in our study. The highest ratio (65%) was detected in Oases and Giza. Due to the small number of patients in NTT and STT procedures separately, the results of the two procedures were combined under the title of STT. Consequently, there were 170 (85%) patients underwent TT and 30 (15%) patients underwent STT. As regards to postoperative clinical complications (Table 2), permanent recurrent laryngeal nerve injury was observed in one (0.6%) patient in TT while temporary injury was observed in 4 (2.4%) and in one (3%) patient in TT and STT respectively. Permanent hypocalcemia was observed in 2 (1%) patients in TT while temporarily hypocalcemia was observed in 10 (5.9%) patients and in one (3%) patient in TT and STT respectively. Permanent hypothyroidism occurred in all patients in TT and 12 (40%) patients in STT. With respect to histologic examination, benign neoplasms were detected incidentally in 8 (4%) cases and they were all follicular adenomas. They were observed equally in 4 patients in both TT and STT (2.4%), (13%) respectively. All adenomas were totally encapsulated, with absent vascular invasion and nuclear atypia. They were all recommended for close follow up without additional surgery. Although undetected during preoperative FNAC, 7 cases (3.5%) of incidental thyroid cancer were detected in both TT and STT. Papillary carcinoma was histologically diagnosed in 5 (3%) patients in TT. All the five patients had no interoperable or radiologic detected lymph nodes enlargement and they required no additional surgery. Papillary carcinoma was also diagnosed during histologic examination in 2(6.7%) patients after STT, and completion thyroidectomy was performed (Table 3). During follow up period, recurrence of goiter was noted in 6 patients (20%) after STT and reoperation was performed for 3 patients and conservative treatment was applied for the remaining 3 patients.

<b>Number of cases</b>	200 (100.00%)
<b>Gender</b>	
Males	40 (20.0%)
Females	160 (80.0%)
<b>Age</b>	
Mean $\pm$ SD	42.65 $\pm$ 7.32
Range	32 – 55
<b>Governorate</b>	
Oasis	70 (35.0%)
Giza	60 (30.0%)
Fayoum	40 (20.0%)
Benisweif	20 (10.0%)
Elmenia	5 (2.5%)
Kaliobia	5 (2.5%)
<b>Operation</b>	
TT	170 (85.0%)
STT	30 (15.0%)

Data were presented as numbers and percentages or mean and standard deviations

TT: Total thyroidectomy; STT: Subtotal thyroidectomy

**Table 1:** Personal and demographic data

Complications/Recurrence	TT	STT	P-value
Permanent recurrent laryngeal nerve injury	1 (0.6%)	0 (0.0%)	0.673
Temporarily recurrent laryngeal nerve injury	4 (2.4%)	1 (3.3%)	0.750
Permanent hypocalcemia	2 (1.2%)	0 (0.0%)	0.550
Temporarily hypocalcemia	10 (5.9%)	1 (3.3%)	0.572
Permanent hypothyroidism	170 (100.0%)	12 (40.0%)	0.000
Recurrent goiter	0 (0.0%)	6 (20.0%)	0.000

TT: Total thyroidectomy; STT: Subtotal thyroidectomy

**Table 2:** Clinical complications and recurrence

Incidental neoplasms	TT	STT	P-value
	No. = 170	No. = 30	
Follicular adenoma	4 (2.4%)	4 (13.3%)	0.004
Papillary carcinoma	5 (2.9%)	2 (6.7%)	0.305

TT: Total thyroidectomy; STT: Subtotal thyroidectomy

**Table 3:** Incidental neoplasms

## Discussion

In the present study, the main target in selecting the surgical protocol for MNG was to avoid discovering of incidental cancer and pathology recurrence. On the other hand, was to leave part of thyroid gland for hormonal supply, to protect the nearby recurrent laryngeal nerve and parathyroid glands. STT, NTT and TT were the conducted surgical procedures. Postoperative clinical complications, incidental cancer and recurrence were the assessed objectives.

Previous comparable studies reported that the surgical management of MNG is still controversial. Many surgical procedures have been recommended such as STT, NTT and TT. STT has been considered the standard surgical treatment for MNG while TT was the standard procedure in thyroid cancer. TT was rarely employed in benign cases because of its high complication rates. However, high recurrence rate despite hormone replacement after STT increased the interest in TT. In recent years, TT has become more acceptable in the treatment of MNG [1-15].

In this study, MNG was much more common in females with female to male ratio 4:1. Five Egyptian governorates were represented in our study. Oasis and Giza recorded the highest ratio (65%) in the conducted demographic study and closer investigation was recommended.

In Egypt, parallel study reported more common incidence of MNG in females with a recorded ratio of 5.6:1. The assessed demographic distribution was higher in rural areas than urban areas [16].

In the present study, 15% of patients underwent STT and NTT procedures for surgical management of MNG. TT was performed in a much higher ratio (85%). TT was the preferable operation by many surgeons and this was chiefly depended on preoperative FNAC and interoperable nodular state of the gland.

Comparable results 52.5% [1], 50% [14], 63% [15], 55% [16] and 61.6% [17] recorded different ratios for TT. They all agreed that the goal of surgical treatment for MNG was to eliminate the disease with a low complication rate and to minimize the necessity for reoperation which increased the risk of permanent complications. TT was appropriate for patients with MNG where there is significant nodular growth involving both lobes [14].

In this study, recurrent laryngeal nerve injury, hypocalcemia and hypothyroidism were the assessed clinical complications. Although permanent complications were not detected in NTT and STT, permanent recurrent laryngeal nerve injury was observed in 0.6 % of patient after TT whereas permanent hypocalcemia was observed in 1% of patients.

Close results were obtained by *Colak et al.*, [1] where permanent recurrent laryngeal nerve injury and permanent hypocalcemia were not observed in any patient with STT. Only in one patient with TT, the recurrent laryngeal nerve injury and hypocalcemia remained permanent.

In the present study, temporarily complications were observed in TT, NTT and STT without significant difference. Temporarily recurrent laryngeal nerve injury was observed in 2.4% of patients and in 3% of patient in TT and STT respectively. Temporarily hypocalcemia was observed in 5.9% of patients and in 3% of patient in TT and STT respectively.

Matching results were obtained by *Colak et al.*, [1] where temporary recurrent laryngeal nerve injury was detected in 9.5% and 6.3% after TT and STT respectively while temporary hypocalcemia was occurred in 11.4% and 9.5% after TT and STT respectively. These reports indicated that performing TT did not result in a higher rate of postoperative complications.

In this study, permanent hypothyroidism and lifelong hormone replacement therapy occurred in all patients after TT and in 40% of patients after STT. *Ozbas et al.*, [5] reported the recommended administration of L-thyroxin in all cases of STT and TT. Therefore, no advantage in performing STT with respect to supplement hormone therapy was proven.

In this study, out of 200 patients underwent thyroidectomy for MNG associated follicular adenomas were histologically detected in 4% of cases. Equal number of adenomas (n=4) were detected after TT compared with NTT and STT. The pathologic examination revealed absent nuclear atypia, capsular and vascular invasion in all cases. Close followed up for the patients were recommended without need for additional surgery.

Matching results were obtained during histopathologic analysis conducted on 165 surgically resected thyroidectomy specimens for MNG. Follicular adenoma was considered the commonest detected benign neoplasm. Two cases (1.2%) of follicular adenoma were accidentally discovered after the surgical operation [18].

In this study, preoperative ultrasound-guided FNAC was performed for all patients in NTT and STT and 20 cases of TT due to the presence of predominant nodules. In 3.5% of patients, FNAC could not help in detecting atypical nuclear features of papillary carcinoma. Papillary carcinoma was detected in 3% of patients after TT while in NTT and STT, 6.7% of patients were histologically diagnosed and completion thyroidectomy was performed.

*Madan et al.*, [14] stated that FNAC was performed in MNG when there was a dominant nodule or suspicion of malignancy. In their study, *Seetu et al.*, [18] clarified that all cases of papillary thyroid micro-carcinoma in MNG were missed by FNAC. A negative FNAC report did not necessarily exclude the possibility of an occult carcinoma, especially in MNG. *Mohammed et al.*, [16] concluded that a correct preoperative assessment, with a careful selection of nodules for FNAC on the basis of ultrasound pattern, could better address the choice of surgical procedure.

In comparable study, the incidence of unsuspected malignancy was 7.4% in STT and 7.6% in TT. The authors emphasized that TT might be preferable treatment modality in patient with huge thyroid gland with higher incidence of malignancy than suspected. They added that a common indication for completion thyroidectomy was incidental carcinoma when a procedure less than TT have been performed [1].

During one year of follow up, 20% of our patients suffered from recurrence of MNG after NTT and STT. Conservative treatment or completion thyroidectomy was accomplished in equal number of patients. However, no neoplasms were observed during the follow up period.

Similar study reported that the risk of recurrence after STT for MNG could be 15%–30% which was quite alarming. The relatively high rate of completion thyroidectomy and its possible complications were supporting performing TT in MNG. The most alarming fact was the appearance of malignant neoplasms in remaining tissue [17].

## Conclusion

The risk of reoperation for incidental cancer and recurrence enhanced the choice of TT as the recommended optimum surgical procedure for MNG.

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