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Outcome of total thyroidectomy in non-malignant solitary thyroid nodule by FNAC

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ABSTRACT

Introduction: Solitary Thyroid Nodules (STN) are a common entity and is detected in approximately 5% to 7% of the adult population by physical examination alone. 7 to 15% of thyroid nodules are harbor cancer. In this study, we will evaluate the outcome of total thyroidectomy in non-malignant STN by FNAC as regards to the histopathological results and post-operative complications. *Patients*

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and methods: This is a prospective randomized control trial study conducted in Ain Shams university hospitals, 30 patients with non-malignant STN by FNAC with a minimal follow up of 12 month after undergoing total thyroidectomy. *Results*: On FNAC, 18 (60%) were benign, 10 (33.3%) were follicular lesion and 2 (6.7%) were Atypia of undetermined significance. complications 5 cases were complicated (16.7%) post operatively. On the final histopathology, 2 cases (6.7%) were confirmed to be malignant both were papillary carcinoma. In Addition, three cases (10%) were found to be hurthle cell tumor. *Conclusion*: Total thyroidectomy seems to be a safe and reliable option for managing patients with solitary thyroid nodules by FNAC as it has low complication rate in experienced hands. Moreover, it obviates the need for completion thyroidectomy.

Keywords: Solitary Thyroid Nodules, thyroidectomy, tumor, follicular lesion, Fine Needle Aspiration Cytology

1. INTRODUCTION

Solitary thyroid nodules are discrete lesions within the thyroid gland. They are radiologically distinct from the surrounding thyroid parenchyma (Haugen et al., 2016). Nodules in the thyroid gland are relatively common, being detected in approximately up to 7% of the adult population on examination. On autopsy, thyroid nodules larger than one centimeter are found with 50% prevalence. They are being found with more frequently, mostly due to the increased use of imaging (Pemayun, 2016). Although more than 90% of detected nodules are clinically insignificant benign lesions, and 7 to 15% of thyroid nodules are harbor cancer (Durante et al., 2015). Ionizing radiation is a known risk factor for both benign and malignant nodules of the thyroid. The risk of developing thyroid nodules is 2% annually. The incidence of malignancy is up to 50% in nodules of previously irradiated thyroids glands (Yeung & Serpell, 2008).

The most commonly used diagnostic techniques for assessing cytopathology of thyroid nodules is the FNAC. The National Cancer Institute recommends using the Bethesda classification which categorizes the findings into 6 outcomes (Cibas & Ali, 2017). The Bethesda system stratifies STN according to FNAC into six categories: Non-diagnostic, Benign, Follicular lesion of undetermined significance (FLUS) or atypia of undetermined significance (AUS), Follicular neoplasm or suspicion for follicular neoplasm, Suspicious for malignancy, Malignancy (Alshaikh et al., 2018). Ways to manage STN include follow up, hemithyroidectomy, total thyroidectomy or radioactive iodine (Jena et al., 2015). Possible post-operative complications include hypocalcemia, RLN plasy, hypothyrodism, bleeding and wound infection. Scar complication could happen like hypertophic scar and keloid (Chahardahmasumi et al., 2019)

2. PATIENTS AND METHODS

This is a prospective randomized control trial study conducted in Ain Shams university hospitals, 30 patients with a minimal follow up of 12 month. An informed consent will be obtained from all patients who will accept to participate (figure 1).

Study duration & period

18 months from January 2018 to July 2019 and the follow up of the patients was a minimum of 12 month.

Inclusion Criteria

1) Fit for Sugery
2) Adult males or females (16 to 70) years old
3) Non Malignant Nodules by FNAC

Exclusion Criteria

1) Generally unfit for surgery
2) Old age (over 70 years old)
3) Malignant Nodules by FNAC
4) Patient refusal

All patients will be subjected to the following: Preoperative assessment

- Full clinical history; personal history, present history, past history
- Full clinical examination;, vital signs, body examination
- Routine preoperative investigations including, complete blood count, random blood sugar, liver function test, kidney function test, coagulation profile, serum electrolytes.

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- Neck Ultrasonography, FNAC of the thyroid nodule, Thyroid profile and Thyroid scan and Thyroid anti-bodies if indicated
- Electrocardiography, Echocardiography and pulmonary function test, if indicated.
- Preoperative co-morbid factors such as hypertension, Diabetes mellitus or electrolyte disturbance will be controlled when possible before surgery

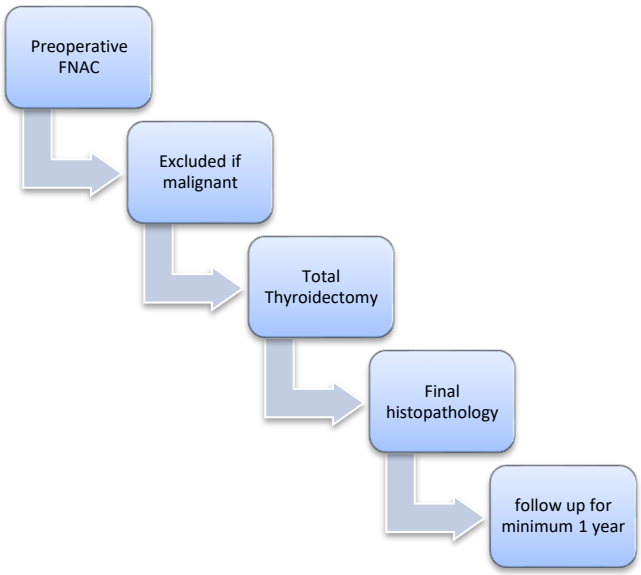

Figure 1 Flow Chart of Methodology

Data collection

Data will be collected from patient records, medical files, and interviews.

Operative Method

Total thyroidectomy was done Kocher incision. We preserved the parathyroid glands (Figure 2) and identified the recurrent laryngeal nerve bilaterally in all cases. A Redivac drain was used routinely.

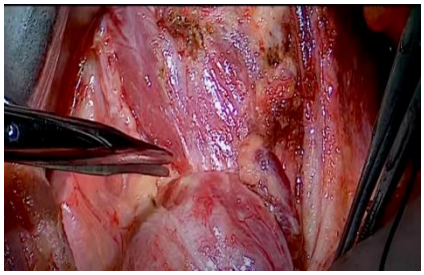

Figure 1: Dissecion of parathyroid gland

Outcome measures

Total thyroidectomy in non-malignant STN by FNAC was assessed in a series of follow up visits over a period of 12 month with the time scale (2 weeks, 1 month, 3 month, 6 month and 12 month). The evaluation will depend on the following points:

- Histopathology
- Postoperative Hypocalcemia
- Recurrent Laryngeal Nerve injur
- Postoperative Bleeding

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- Rate of Recurrence

Statistical analysis

The collected data will be revised, coded, tabulated and introduced to the PC using Statistical Package for Social Science SPSS. Data will be presented and suitable analysis will be done according to the type of data obtained for each parameter.

3. RESULTS

In this study we had 30 patients ranging from 18 to 60 years old the mean age was 33.97 ±11.44. 20 (66.7%) patients were females whilst only 10 (33.3%).28 (93.3%) were euthyroid whilst only 2 (6.7%) were hypothyroid and none were hyperthyroid (Table 1)

Table 1: Demographics of the cases

		No. = 30
Age	Mean±SD	33.97 ± 11.44
	Range	18 – 60
Sex	Female	20 (66.7%)
	Male	10 (33.3%)

On FNAC, 18 (60%) were benign, 10 (33.3%) were follicular lesions and 2 cases (6.7%) were Atypia of undetermined significance (Figure 2). On Ultrasonography, 20 (66.7%) showed TIRADS 3, 9 (30%) showed TIRADS 4 and only 1 (3.3%) showed TIRADS 5. The nodule sizes ranged from 13 to 28 mm with mean 20.00±4.00 mm. ENT consultation was done for all cases preoperatively and all had bilateral mobile vocal cords. The operation lasted from 70 to 110 minutes with a mean 90.50±9.94 minutes.

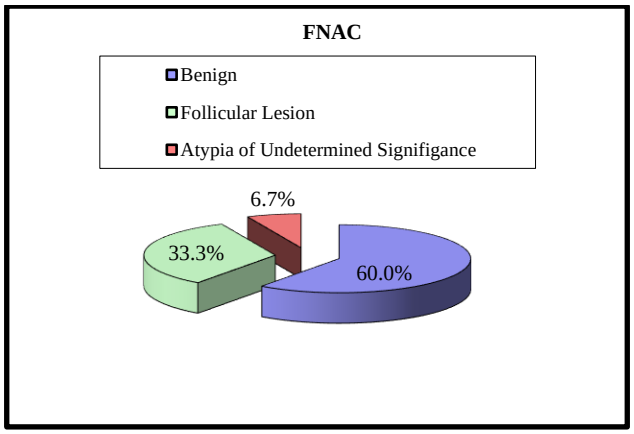

Figure 2: Preoperative FNAC distribution

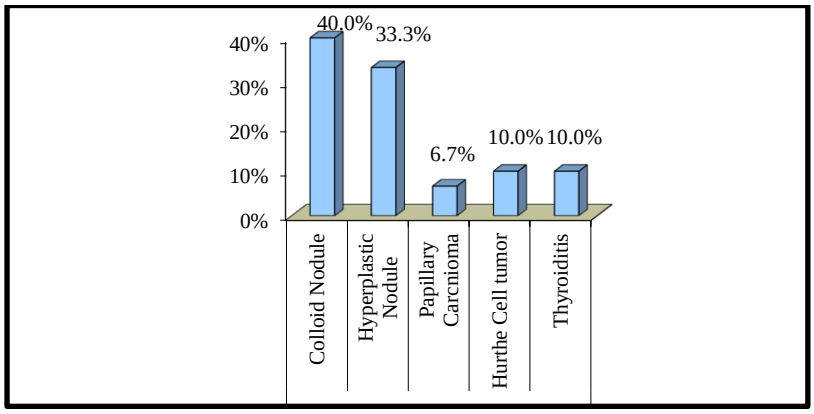

Figure 3 Final Histopathology distribution

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On the final histopathology, 25 out of the 30 cases (83.33%) were found to be benign: 12 (40%) be colloid nodules, 10 (33%) hyperplastic nodules, 3 (10%) thyroiditis.2 cases (6.7%) were confirmed to be malignant both were papillary carcinoma.3 cases (10%) were hurthle cell tumor, they didn't show any evidence of malignancy as capsular or lymph-vascular invasion or metastasis (Figure 3).

The mean hospital stay was 2.40 ± 1.25 and the all cases stayed from 2 to 7 days. As regards to overall post-operative complications, 5 cases were complicated (16.7%).3 cases (10%) showed post-operative hypocalcemia all of them were temporary and resolved within a week.2 cases (6.7%) had post-operative recurrent laryngeal nerve palsy all of which were transient and resolved with maximum 6 weeks. None of the cases developed wound infection, postoperative bleeding or hypothyroidism (Table 2)

Table 2 Post-operative complications number and percentages

Postoperative complications		**No.**	**%**
Negative		25	83.3%
Positive		5	16.7%
Hypocalcemia	No	27	90.0%
	Yes	3	10.0%
RLN injury	No	28	93.3%
	Yes	2	6.7%
Hypothyroidism	No	30	100.0%
	Yes	0	0.0%
Wound infection	No Yes	30 0	100.0% 0.0%
Bleeding	No	30	100.0%
	Yes	0	0.0%

2 cases (6.7%) were found to be multinodular goitres on histopathology instead of being goitres of solitary thyroid nodules as considered clinically and radiologically. A single patient (3.3%) needed a second surgery in the form of lateral neck dissection.(Table 3). 4 (13.3%) patient had scar complications. 3 (10%) had hypertrophic scars and 1 (3.3%) had a keloid scar (Table 4).

Table 3 Miscellaneous findings

Multinodlular on final histopathology	No	28	93.3%
	Yes	2	6.7%
Second Surgery	No	29	96.7%
	Yes	1	3.3%

Table 4 Scar complications numbers and percentages

Scar complications			
Hypertrophic scar	No	27	90.0%
	Yes	3	10.0%
Keloid	No	29	96.7%
	Yes	1	3.3%

There was zero mortality in our cases and none of the cases developed recurrence during our follow up period of 12 month.

4. DISCUSSION

Solitary thyroid nodules are discrete lesions within the thyroid gland. They are radiologically distinct from the surrounding thyroid parenchyma (Haugen et al., 2016). Although more than 90% of detected nodules are clinically insignificant benign lesions, and 7 to 15% of thyroid nodules are harbor cancer (Pemayun TG 2016). Also there is an established risk of malignancy up to 75% even in nodules not confirmed to be malignant by FNAC (Haugen BR et al., 2016), so thyroid cancer can be found incidentally in the final specimen like the 2 cases (6.7%) of papillary carcinoma we found (Cibas & Ali 2017). Solitary thyroid nodules are evaluated mainly

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with thyroid profile, neck ultrasonography and fine needle aspiration cytology, which guide to the line of management that could usually follow up, hemithyroidectomy, total thyroidectomy or radioactive iodine.

In our study we did total thyroidectomy to all our patients who had non malignant solitary thyroid nodules by FNAC. In this study we had 30 patients ranging from 18 to 60 years old the mean age was 33.97 ±11.44. 20 (66.7%) patients were females whilst only 10 (33.3%) were males affirming the literature that solitary thyroid nodule is more common in females. Tai et al. found solitary nodules 4 times more frequently in women than in men (Chahardahmasumi et al., 2019; Tai et al 2012). 28 (93.3%) were euthyroid whilst only 2 (6.7%) were hypothyroid and none were hyperthyroid. Other papers reported similar results. On FNAC, 18 (60%) were benign, 10 (33.3%) were follicular lesion and 2 (6.7%) were Atypia of undetermined significance.20 (66.7%) showed TIRADS 3, 9 (30%) showed TIRADS 4 and only 1 (3.3%) showed TIRADS 5. The nodule sizes ranged from 13 to 28 mm with mean 20.00 ± 4.00 mm. Uyar et al. reported an average of 22.6 ± 12.2 (Tandri & Mahesh 2019; Uyar, 2017). All cases had mobile vocal cords documented preoperatively. The operation lasted from 70 to 110 minutes with a mean 90.50 ± 9.94 minutes. Arnaud et. al. found average operative time was 86 minutes (Arnaud et al., 2017). On the final histopathology result 25 out of the 30 cases (83.33%) were found to be benign: 12 (40%) be colloid nodules, 10 (33.%) hyperplastic nodules, 3 (10%) thyroiditis.2 cases (6.7%) were confirmed to be malignant both were papillary carcinoma. 3 cases (10%) were hurthle cell tumor, they didn't show any evidence of malignancy as capsular or lymph-vascular invasion or metastasis. But the distinction between benign and malignant hurthle cell tumors is not very clear. For this reason, many surgeons advocate total thyroidectomy for it (Cannon, 2011).

Uyar et al reported 19% colloid, 9 % hyperplastic, thyroiditis 9.9%, 35% for papillary carcinoma and hurthle cell tumor 5.7% (Uyar, 2017). The mean hospital stay was 2.40 ± 1.25 and the all cases stayed from 2 to 7 days. As regards to overall post-operative complications, 5 cases were complicated (16.7%). Khanzada et al. found 10% overall complication rate. 3 cases (10%) showed post-operative hypocalcemia all of them were temporary and resolved within a week.Pathan et al. 2019 reported 14%. 2 cases (6.7%) had post-operative recurrent laryngeal nerve palsy all of which were transient and resolved with maximium 6 weeks. Pathan et al. reported 5.5% (Khanzada et al., 2010; Pathan et al., 2019). None of the cases had any postoperative bleeding. Calò et al. reported 6.5% and also non cases developed wound infection while Chahardahmasumi et al., reported 3.4% (Calò et al., 2010; Chahardahmasumi et al., 2019).

Zero cases developed hypothyroidism. We started replacement therapy as soon as the final histopathology was available. Danese et al reported that it happen in 14-75% of cases (Danese, 1996). 2 cases (6.7%) were found to be multinodulargoitres on histopathology instead of being goitres of solitary thyroid nodules as considered clinically and radiologically. Welker and Orlov found 23% to be so. One patient (3.3%) needed a second surgery in the form of lateral neck dissection (Welker & Orlov, 2003). 4 (13.3%) patient had scar complications. 3 (10%) had hypertrophic scars and 1 (3.3%) had a keloid scar. Also, there was a significant relation between hurthle cell tumor and follicular lesion. As all patients who were found out to have hurthle cell tumor on their final report had a follicular lesion on FNAC. And 3 out of the 10 patients (30%) who had this finding on their preoperative FNAC were found to be hurthle cell tumor later on. P-Value was 0.036. There was zero mortality in our cases and none of the cases developed recurrence during our follow up period of 12 month. For fear of malignancy, patients who undergo surveillance for a STN need a meticulous serial follow up and observation for the size of the nodule, also those who had a lobectomy done to them need to be followed up carefully for the other lobe and may need a completion thyroidectomy. A high drop-out rate happens to appear in our institute for follow up. In addition, many patients don't come back for second surgery are satisfied with only hemithyroidectomy. The risk of this is decreased by performing total thyroidectomy from the start. As there is no residual thyroid tissue after total thyroidectomy, patients can benefit from radioactive iodine ablation, do thyroid scans or whole body scans (Andresen et al., 2017). It also allows follow up using thyroglobulins as tumor markers. After total thyroidectomy, theoretically, the level has to drop to zero because no thyroid tissue is expected to be left behind after surgery. Persistent of TG after total thyroidectomy means that there is residual thyroid tissue at the thyroid bed, local or distant metastases (Indrasena, 2017). Total thyroidectomy avoids the need of for completion thyroidectomy with its high complication rate reaching up to 42%. It is sometimes needed in case of incidental malignancy after lobectomy (Gulcelik et al., 2012). In addition we have found 3 cases (10%) of Hurthle cell tumor on final histopathology which is deemed by many as an indication for total thyroidectomy.

5. CONCLUSION

In light of our results, Total thyroidectomy seems to be a safe and reliable option for managing patients with non-malignant solitary thyroid nodules by FNAC as it has low complication rate in experienced hands. Moreover, it obviates the need for completion thyroidectomy which has a high complication rate and sometimes patients don't comeback for it and are satisfied with only hemithyroidectomy. Also it allows easier follow up of the patient post operatively radiologically and by markers and to take

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radioactive iodine for diagnostic and therapeutic reasons if needed. Furthermore, prevents the patients from needing the serial follow up needed if the nodules are managed by surveillance or hemithyroidectomy.

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We thank the patients who participated in and contributed samples to the study.

Abbreviations
STN: Solitary Thyroid nodule
FNAC: Fine Needle Aspiration Cytology
RLN: Recurrent Laryngeal Nerve
SSPS: Statistical Package for Social Science
TIRADS: Thyroid Imaging Reporting and Data System
TG: Thyroglobulin

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Author Contributions
1. Yahya Zakaria Mohamed Ali Abou El-Wafa: Collected the data and Conceived and designed the analysis and wrote the paper
2. Dr. Hisham Mohamed Omran: Supervised the whole process
3. Dr. Ahmed Yasser Elrifai: Supervised the whole process
4. Prof. Dr. Nafissa El-Badawy: Supervised the whole process specifically the FNAC and histopatholgy sampling and reporting.
5. Prof. Dr. Mahmoud Ahmed El-Shafei: Supervised the whole process.

Informed consent
Written & Oral informed consent was obtained from all individual participants included in the study. Additional informed consent was obtained from all individual participants for whom identifying information is included in this manuscript.

Conflicts of interest
There are no conflicts of interest

Data and materials availability
All data associated with this study are present in the paper

Ethical approval for study protocol
The study was approved by the Medical Ethics Committee of Ain Shams University (ethical approval code: 0006379).

Peer-review
External peer-review was done through double-blind method.

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