A Prospective Observational Study Assessing the Relationship Between Solitary Thyroid Nodule Size and Incidence of Malignancy

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Abstract

Background
Solitary thyroid nodule (STN) is a well-documented entity. Autopsy data indicate a 50% prevalence of thyroid nodules >10 mm in patients without clinical evidence of thyroid disease. Prevalence of palpable nodules is 4-7%. Solitary thyroid nodules are often asymptomatic and found incidentally. Fine needle aspiration cytology is recommended to determine the nature of the thyroid nodule. 5-10% of the thyroid nodules are found to be malignant following thyroidectomy.

Objective
Our study aims to explore the relationship between solitary thyroid nodule size and malignancy.

Methods
A prospective, observational analysis looking at preoperative thyroid ultrasound scan findings and post-operative histology for a total of 100 female patients referred to our unit within a university hospital from November 2016 to April 2019. Statistical analysis including One-Way ANOVA was performed where appropriate.

Results
Total number of patients was 100 female patients divided according to the size of the nodule into three groups with the correlation between the size of the nodule and the incidence of malignancy.

Group A: Patients with a STN <20 mm; eight patients; post-operative histology = all benign.

Group B: Patients with a STN measuring 20-40 mm; 80 patients: 68 patients were benign, and 12 patients (12%) were malignant (incidence of malignancy in the group is 15%).

Group C: Patients with a STN >40 mm; 12 patients: eight patients were benign, four patients were malignant, (incidence of malignancy = 33%).

Correlation between the size of the nodule and the incidence of malignancy:
Group A: 0/8 malignancy; Group B: 12/80 patients were malignant; Group C: 4/12 malignant.

Conclusion
Our results suggest that the size of a solitary thyroid nodule cannot be reliably used for at predicting malignancy and should not be influencing patient’s management.

Categories: Endocrinology/Diabetes/Metabolism, General Surgery
Keywords: thyroid, solitary thyroid nodule, ultrasound scan, thyroid cancer

Introduction
Solitary thyroid nodule is a common entity with autopsy data indicating a prevalence of 50% in patients with nodules larger than 1 cm without clinical evidence of thyroid disease. The prevalence of palpable nodules is 4-7% [1, 2].

Thyroid nodules warrant removal when they are large enough to be symptomatic, or if there is a concern for
malignancy. The majority of nodules are asymptomatic. With 5–10% of nodules being malignant, the decision to operate is made on therapeutic or diagnostic grounds [3, 4].

Most patients present with a large palpable thyroid nodule. However, some solitary thyroid nodules are incidentally found on imaging studies performed for other reasons [5].

Barroeta et al. found that a single dominant or solitary nodule is more likely to represent carcinoma than a single nodule within a multi-nodular gland. The incidence of malignancy increased from 2.7 to 30% and from 1.4 to 10%, respectively [6].

Important elements in a patient’s history increase the likelihood of malignancy, these include prior head and neck irradiation, rapid nodule growth, dysphagia, dysphonia, male gender, presentation at extremes of age (<20 years or >70 years) and family history of medullary thyroid carcinoma or multiple endocrine neoplasia [7,8].

**Aim of our study**

This study aims to determine the relationship between size and the incidence of malignancy in patients with a solitary thyroid nodule.

**Materials And Methods**

We conducted a prospective, observational analysis looking at preoperative thyroid ultrasound scan findings and post-operative histology for a total of 100 female patients referred to our unit within a university hospital from November 2016 to April 2019.

The study was approved by the local medical ethics committee. Inclusion criteria: female patients only (to eliminate sex-related bias) who were found to have a solitary thyroid nodule on neck ultrasound scan. All selected patients were euthyroid and fit for general anaesthesia. Exclusion criteria: male patients, patients with diffusely enlarged thyroid gland, patients not fit for general anaesthesia, recurrent cases and patients with thyrotoxicosis.

All patients were euthyroid on preoperative blood tests and underwent a preoperative neck ultrasound scan and an ultrasound-guided fine-needle aspiration cytology (FNAC).

**Statistical analysis**

Data were collected and coded to facilitate data manipulation and double entered into Microsoft Access and data analysis was performed using Statistical Package of Social Science (SPSS) software version 18 (IBM Corp., Armonk, NY) in windows 7.

**Results**

Total number of patients included in our analysis was 100 patients; their age range was 20-55 years with mean ± SD 33 ± 9.5 years, 56 patients (56%) were younger than 30 years, 28 patients (28%) were 30-40 years, 12 patients (12%) were 40-50 years and four patients (4%) were older than 50 (Table 1).

| Age       | No. | %  |
|-----------|-----|----|
| <30 y     | 56  | 56%|
| 30-40 y   | 28  | 28%|
| 40-50 y   | 12  | 12%|
| >50 y     | 4   | 4% |
| Total     | 100 | 100%|
| Min.-Max. | 20-55 ys |    |
| Mean ± SD | 33.0 ± 9.5 yrs |    |

**TABLE 1: Distribution of studied sample according to patient’s age**

Patients were divided according to the maximum diameter size of the solitary thyroid nodule on ultrasound scan. Similar categories were used for both pre-operative and post-operative size: group (A): less than 20
mm, group (B): 20-40 mm, and group (C) greater than 40 mm. Pre-operative ultrasound and post-operative histopathology reports demonstrated minimal difference ±1-2 mm between the two groups (Table 2).

| Nodule size in each group   | Size by US | Size in post-operative pathology |
|-----------------------------|-----------|----------------------------------|
| Group (A): size < 2 cm      | 8 (8%)    | 8 (8%)                           |
| Group (B): size 2-4 cm      | 80 (80%)  | 80 (80%)                         |
| Group (C): size >4 cm       | 12 (12%)  | 12 (12%)                         |
| Total                       | 100 (100%)| 100 (100%)                       |
| Min.-Max.                   | 1.5 cm-5 cm|                                  |
| Mean ± S.D.                 | 3.5 cm ± 1.5 cm |                              |

**TABLE 2: Distribution of the studied sample according to the nodule size in preoperative ultrasound (US) compared to nodule size in postoperative histopathology reports.**

Pre-operative FNAC revealed that 20 patients (20%) had colloid adenoma, 48 patients (48%) had a follicular lesion, 28 patients (28%) had papillary adenoma, four patients (4%) had papillary thyroid carcinoma (Table 3).

| Pre-operative FNAC            | Number | %    |
|-------------------------------|--------|------|
| Colloid adenoma               | 20     | 20%  |
| Follicular lesion             | 48     | 48%  |
| Papillary adenoma             | 28     | 28%  |
| Papillary carcinoma           | 4      | 4%   |
| Total                         | 100    | 100% |

**TABLE 3: Distribution of studied sample according to pre-operative FNAC results.**

FNAC: Fine-needle aspiration cytology

A total of 80 patients (80%) had hemi-thyroidectomy of the affected lobe. Exploration of the contralateral lobe was carried out for all patients. Fine nodularity was found in 20 patients (20%). Total thyroidectomy with lymph node dissection was carried out for the four patients with carcinoma.

Post-operative histopathology results were divided into two groups:

Benign: 84 patients (84%) - 20 colloid adenoma, 36 follicular adenoma, 20 patients (20%) were papillary adenoma and eight patients (8%) were papillary adenoma with cystic degeneration; Malignant: 16 patients (16%) - 12 follicular carcinoma and four papillary carcinomas (Table 4).
TABLE 4: Distribution of studied sample according to patient's post-operative histopathology.

| Post-operative histopathology            | No | %  |
|------------------------------------------|----|----|
| Colloid adenoma                          | 20 | 20%|
| Follicular adenoma                       | 36 | 36%|
| Papillary adenoma                        | 20 | 20%|
| Papillary adenoma & cystic degeneration  | 8  | 8% |
| Follicular carcinoma                     | 12 | 12%|
| Papillary carcinoma                      | 4  | 4% |
| Total                                    | 100| 100%|

Correlation between the size of the nodule and the incidence of malignancy:

- Group A: 0/8 malignancy. Group B: 12/80 patients were malignant. Group C: 4/12 malignant (Table 5).

TABLE 5: Distribution of studied sample according to patient's post-operative histopathology in correlation with the incidence of malignancy.

* The percentage to the total number in the study (n = 100)

**Groups of nodule size**

| Groups of nodule size | Benign No. (%) | Malignant No. (%) |
|-----------------------|----------------|-------------------|
| Group A: <20 mm       | 8 patients (8%)* | 0 (0%)*           |
| Group B: 20-40 mm     | 68 patients (68%)* | 12 patients (12%)* |
| Group C: >40 mm       | 8 patients (8%)* | 4 patients (4%)*  |

Discussion

Thyroid nodules are observed in 8% of the adult population and seen more frequently in women than men. A solitary thyroid nodule is defined clinically as a localized thyroid enlargement with an apparently normal remaining gland. Such nodules carry a 5-15% prevalence of malignancy. Thyroid malignancies account for approximately 1% of all malignant neoplasms and are the most common endocrine neoplasia. With the use of ultrasound, up to 10 times more nodules are thought to be detected. They are found in 4%-8% of adults by palpation and in 13%-67% when ultrasound detection is utilized. In autopsy studies, they have a prevalence of approximately 50% [9-11].

Tai Jun et al. concluded that male gender, microcalcification and lymphadenopathy are independent risk factors for predicting malignancy in patients with STN; patients with more than two of those risk factors should be subjected to further examination or thyroidectomy [9].

Some studies suggested that the size of a solitary thyroid nodule can be considered as an independent predictor for risk of malignancy, especially in the presence of underlying risk factor. McCoy et al. concluded that due to high false-negative rate for preoperative benign cytology, thyroid nodules greater than or equal to 4 cm should be considered for diagnostic lobectomy regardless of fine-needle aspiration biopsy (FNAB).
operative workup to ensure potential malignancies are not missed. We recommend a multicentric study Nevertheless, size of STN cannot be reliably used for predicting malignancy; we advocate thorough pre-operative fine-needle aspiration cytology findings. Our results suggest that increasing size of a solitary thyroid nodule and the risk of malignancy.

Management of solitary thyroid nodules is based on clinical assessment, ultrasound scan findings and preoperative fine-needle aspiration cytology findings. Our results suggest that increasing size of a solitary thyroid nodule may be a predictor for malignancy.

Nevertheless, size of STN cannot be reliably used for predicting malignancy; we advocate thorough pre-operative workup to ensure potential malignancies are not missed. We recommend a multicentric study
Additional Information

Disclosures

**Human subjects:** Consent was obtained by all participants in this study. Fayoum University Hospital medical ethics committee issued approval. Not applicable. The study was approved by the medical ethics committee at Fayoum University Hospital. **Animal subjects:** All authors have confirmed that this study did not involve animal subjects or tissue. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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