

## Serum Thyrotropin Concentration as a Predictor of Malignancy in Thyroid Follicular Neoplasm

Seyyed Morteza Taghavi\* and Reyhaneth Takallu

Endocrine research centre, Massad Medical university, Iran

### Abstract

**Objective:** The clinical importance of thyroid nodules is the need to exclude thyroid malignancy, and fine-needle aspiration biopsy (FNAB) is the current gold standard for the evaluation of thyroid nodules. The main limitation of FNAB is follicular neoplasm. Follicular thyroid carcinoma differentiates less frequently with FNAB from microfollicular or cellular adenomas. Serum TSH is introduced recently as a useful marker for predicting malignancy in a thyroid nodule. The main aim of our study was the evaluation of this correlation in patients with thyroid nodule with cytology reports of follicular neoplasm, in them the final diagnosis of benign or malignant disease confirmed histologically after surgery.

**Method:** We prospectively collected data on 75 patients including 64 females and 11 males presenting with thyroid nodule with cytology report of follicular neoplasm. A primary evaluation was performed at presentation through measurement of T4, T3, and TSH concentrations and thyroid radioisotope scan. A final histological diagnosis was made in all patients after thyroid surgery. The influence of factors including age, gender, size and location of nodules, and serum TSH concentration on the final diagnostic outcome was investigated statistically.

**Results:** In 42 patients (56%), the nodule was on right lobe, in 30 patients (40%), the nodule was on left lobe and in 3 patients (4%), on isthmus. Mean age was  $37.6 \pm 11.36$  (15-68) years. Mean size of nodules was  $18.4 \pm 17.48$  mm. Mean TSH was  $0.9 \pm 1.29$  mU/liter. After surgery, malignancy was confirmed in 19 (25.3%) patients. In 38 patients (50.7%), final pathology was follicular adenoma and in 18 (24%), it was multinodular goiter. There was no correlation between sex, age, size and location of nodule and malignancy. Mean TSH was significantly higher in cancer patients.

**Conclusion:** The serum TSH concentration at presentation is an independent predictor of the presence of thyroid malignancy in patients with follicular neoplasm.

**Keywords:** Thyrotropin (TSH); Follicular neoplasm; Thyroid nodule; Thyroid cancer

### Introduction

The clinical importance of thyroid nodules is primarily the need to exclude thyroid malignancy, which accounts for 4 to 6.5 percent of all thyroid nodules [1-4]. Although several imaging modalities are available, fine-needle aspiration biopsy (FNAB) is the current gold standard for the diagnosis of patients presenting with thyroid nodules [5,6]. Unlike for papillary thyroid carcinoma, follicular thyroid carcinoma is being differentiated less frequently with FNAB from microfollicular or cellular adenomas. These specimens which accounts for 20 percent of all thyroid biopsies are usually categorized as follicular neoplasm [7,8]. Most physicians recommend surgery in these patients and final diagnosis of follicular cancer is made on the basis of capsular or vascular invasion evidences after surgical excision of thyroid nodule.

Many studies were performed to develop clinical (gender, nodule size, character of the gland by palpation) or paraclinical (PET scans, RT-PCR measurement of thyroglobulin mRNA, cellular and molecular markers) criteria that improve upon cytology to predict malignancy in follicular neoplasm [9-19].

Serum TSH is introduced recently as a useful marker for predicting malignancy in a thyroid nodule [20-25]. The main aim of our study was the evaluation of this correlation in patients with thyroid nodule with cytology reports of follicular neoplasm, in them the final diagnosis of benign or malignant disease was confirmed histologically after surgery.

### Method

We prospectively collected data on 75 patients presented with thyroid

nodule with cytology report of follicular neoplasm to the Thyroid Clinic at the Ghaem University Hospital, Mashhad, Iran, between April 2007 and December 2011. The subjects included 64 females and 11 males with a mean age of 37.6 yr (range 15–68 yr). A biochemical evaluation was performed at presentation through measurement of T4, T3, and TSH concentrations. A final histological diagnosis was made in all patients after thyroid surgery. The final diagnostic outcome was defined as the presence or absence of malignancy. The influence of factors including age, gender, size and location of nodules, and serum TSH concentration on the final diagnostic outcome was investigated statistically. Data were descriptively expressed as mean  $\pm$  SD or number and percent. Data were analyzed using the Student's *t*-test, chi-square by statistical software SPSS version 11.5. A P value below 0.05 was considered statistically significant. All subjects have given their informed consent and the Endocrine Research Committee of Mashhad University reviewed all aspects of the research and approved the protocol.

**\*Corresponding author:** Seyyed Morteza taghavi, Endocrinologist, Assistant professor of Endocrinology, Endocrine research centre, Massad Medical university, Ahmad Abad Street, Ghaem Hospital, Mashhad, Iran, Tel: 00989155164037; Fax: 00985118406757; E-mail: taghaviMR@mums.ac.ir

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## Results

The subjects were 75 patients including 64 women (85.3%) and 11 men (14.7%). In 42 patients (56%) the nodule was on right lobe, in 30 patients (40%) was on left lobe and in 3 patients (4%) on isthmus. Mean age was  $37.6 \pm 11.36$  (15-68) years. Mean size of nodules was  $18.4 \pm 17.48$  mm. Mean TSH was  $0.9 \pm 1.29$  (between 0.3-4.5) mU/liter. In all of the patients cytology report was follicular neoplasm. After surgery, malignancy was confirmed in 19 (25.3%) patients. In 38 patients (50.7%) final pathology was follicular adenoma and in 18 (24%) was multinodular goiter. There was no correlation between sex ( $P=0.097$ ), age ( $P=0.0966$ ), size ( $P=0.396$ ) and location ( $P=0.127$ ) of nodule and malignancy. Mean TSH was significantly higher in cancer patients ( $P=0.0001$ ). Using Receiver operating characteristic (ROC) curves a cutoff value of 0.85mU/l determined for serum TSH level in differentiation of malignant and benign nodules. The sensitivity of this value was 84% and the specificity of it was 85.7%.

## Discussion

Thyroid cancer, the most common endocrine malignancy usually presents as a solitary nodule. FNAB is the best way for the diagnosis of cancer in patients presenting with thyroid nodules [5,6]. FNA cytology reports are classified as: Benign, Follicular lesion of undetermined significance and Follicular neoplasm, Suspicious for malignancy, Malignant and Nondiagnostic [26]. Unlike for papillary thyroid cancer, FNA biopsy cannot differentiate follicular thyroid cancer from follicular adenomas. These specimens are usually reported as indeterminate lesions, categorized as follicular neoplasm or follicular lesions of undetermined significance [7,8]. Pathologic evaluation of the thyroid after surgery confirms the actual diagnosis of follicular thyroid cancer. Treatment in benign and malignant group is straightforward, but in patients with cytology suggesting follicular neoplasm is controversial. Physicians usually perform thyroid scintigraphy and most patients with non autonomous adenomas should undergo surgery because 15 to 25 percent of them prove to be cancers [26]. Many procedures are under investigation to improve the diagnostic value of cytology alone for the assessment of follicular neoplasm. These include RT-PCR measurement of thyroglobulin mRNA, PET scans, cellular and molecular markers [9-19]. More recently, many studies have suggested that Serum TSH is an independent risk factor for predicting malignancy in a thyroid nodule [20-25]. Higher serum TSH levels also have been associated with advanced stages of thyroid cancer [23]. Many data support the role of TSH in thyroid cancer. Many studies have shown higher incidence of thyroid cancer in patients with Hashimoto's thyroiditis and Graves' disease, compared with control population [27,28]. Elevated TSH due to continuous progression to hypothyroidism in Hashimoto's disease and TSH receptor stimulation by TSH receptor antibody in Graves' disease may explain the higher rate of malignancy in these patients. The trophic effect of TSH on thyroid cancer growth also is well established [29,30] and TSH suppression by administering exogenous thyroid hormone is an independent predictor of recurrence of differentiated thyroid cancer [31]. An alternative explanation is that patients with lower TSH concentrations were developing autonomous function, which by itself is associated with lower rates of malignancy [32-34].

In this study it is demonstrated that the presenting serum TSH concentration is also a useful parameter in the prediction of probability of underlying malignancy in follicular neoplasm.

## Conclusion

For the first time, we have demonstrated that the serum TSH

concentration at presentation is an independent predictor of the presence of thyroid malignancy in patients with follicular neoplasm.

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## Declaration of Competing Interests

No competing financial interests exist.

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