The Relationship of Clinicopathological Factors of the Tumor with Preoperative TSH Level in Papillary Thyroid Cancers

Evren Besler¹, Bulent Citgez¹, Nurcihan Aygun¹, Mustafa Fevzi Celayir¹, Müveddet Banu Yılmaz Ozguven², Mehmet Mihmanli¹, Sitki Gurkan Yetkin¹, Mehmet Uludag¹

ABSTRACT

Objective: Thyroid-stimulating hormone/thyrotropin (TSH) is known to induce malignancies and tissue growth of the thyroid gland. While the relationship of higher levels of TSH with advanced stages of cancer had been published in previous studies, the relationship of the tumor with the clinicopathological factors had not been completely evaluated. The aim of the present study was to evaluate the relationship between highly risky clinicopathological factors with preoperative high levels of TSH.

Materials and Methods: The records of 89 patients (67 females and 22 males) who underwent surgery for differentiated thyroid cancer between 2011 and 2013 were reviewed. The relationship of preoperative TSH between tumor size, multicentricity, lymphovascular invasion, extrathyroidal extension, central neck metastasis, and lateral neck metastasis was evaluated.

Results: The preoperative TSH levels were high in patients with multicentricity (p=0.022), lymphovascular invasion (p=0.018), and central neck metastasis (p=0.002). The prevalence of extrathyroidal extension (p=0.41), lymphovascular invasion (p=0.020), and central metastasis (p=0.009) was significantly high in patients with a TSH level ≥2.5 mIU/L. The preoperative TSH levels were determined as an independent predictive risk factor for central neck metastases (p=0.012) and extrathyroidal extension (p=0.041) in multinomial logistical regression analysis.

Conclusion: The power of radiological imaging for the identification of central neck metastases in preoperative evaluation is limited. The preoperative high level of TSH is an independent predictive factor for central metastases and extrathyroidal extension. It can help to predict tumor staging. Furthermore, related with multicentricity and lymphovascular invasion, it can affect the high risk characteristics of the tumor except the stage. The preoperative TSH level can be considered for the probability of preoperative metastases and can contribute to plan the extent of surgery.

Keywords: Clinicopathological factors, thyroid cancer, thyrotropin/thyroid-stimulating hormone

Introduction

Thyroid cancer is the most frequent endocrine malignancy [1]. The outstanding clinical parameters associated with an increased risk of malignant disease of age (<20 and >70 years), male sex, solitary nodule, node size of >4 cm, rapid nodular growth, and radiation exposure history are well known [2].

Thyrotropin (TSH) is a well-accepted thyrocyte growth factor [3]. The relationship of the TSH with differentiated thyroid cancer (DTC) was evaluated several times in previous studies. In previous studies, the increasing risk of thyroid malignancy in thyroid nodules by the higher levels of TSH has been emphasized [4–11]. In recent studies, the relationship between the tumor size and the TSH level is further examined [12–14]. In a recent meta-analysis, a higher serum TSH level involved higher risk of papillary thyroid cancer (PTC) [15]. In a study, TSH receptor expression was found to be an independent factor that affects the prognosis of patients with PTC [16].

Overall, the relationship of clinicopathological factors of the tumor with TSH level and its contribution to preoperative surgical assessment are not fully examined until today. The aim of the present study was to evaluate the relationship between highly risky clinicopathological factors with preoperative high levels of TSH.

Materials and Methods

We examined the records of 89 patients (67 females and 22 males) who underwent surgery for thyroid cancer between 2011 and 2013 retrospectively. The mean age of the patients was
50.7 (20–80) years. In all patients, preoperative ultrasonography (USG), TSH levels, and thyroid function tests were evaluated. Fine needle aspiration biopsy (FNAB) was applied to patients according to the USG findings of the nodules. Patients who were suspected of malignancy in the FNAB results were additionally evaluated with USG for central and lateral neck metastasis. Patients who were suspected clinically or suspected of extrathyroidal extension to the adjacent organ spread were additionally evaluated with magnetic resonance imaging and computed tomography. The FNAB procedure was applied to the lateral neck lymphatic nodes that were suspected of metastasis and confirmed. Preoperative serum TSH values were measured, and the results were recorded in mIU/L. A level of ≥2.5 mIU/L is considered as high. Patients who had antithyroid treatment before surgery were excluded from the study.

All patients underwent surgery conducted by the same endocrine surgeon. In cases with a unifocal intrathyroidal microcarcinoma (<1 cm in diameter) and without cervical lymph node involvement, thyroid lobectomy with isthmusectomy was performed. Total thyroidectomy was primarily performed in other cases. The dissection of the central neck area was performed when there was an enlarged lymph node in preoperative imaging studies or palpated in the central neck region peroperatively. Prophylactic central neck dissection was applied to the cases with a tumor size >4 cm. Neck dissection was performed from levels II to V in case of metastasis to the lateral compartment of the neck in the preoperative evaluation and also in time following thyroid surgery. The dissection descriptions of the central region were performed according to the consensus report of the American Thyroid Association Surgery Working Group [17].

The histopathological parameters of each specimen were evaluated by the same pathologist. All pathological specimens were analyzed for primary tumor size, multifocality/multicentricity, extrathyroidal extension, and cervical (central and lateral) lymph node metastasis (LNM). The specimens were classified according to the tumor, lymph node, and metastasis (TNM) staging system of the 7th edition of the Union for International Cancer Control and the American Joint Committee on Cancer and according to the well-established prognosis classification system of DTC, age, metastasis, extent, and size stage system [18].

By analyzing the specimen reports, the relationship of preoperative TSH between tumor size, multifocality/multicentricity, extrathyroidal extension, central neck metastasis, and lateral neck metastasis was evaluated. The approval of the ethical committee of Istanbul Health Sciences University Şişli Hamidiye Etfal Training and Research Hospital was obtained to conduct the study. Informed consent was obtained from the patients prior to the study.

<table>
<thead>
<tr>
<th>Table 1. The clinicopathological factors and preoperative TSH level</th>
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<tbody>
<tr>
<td>Clinical and pathological properties</td>
</tr>
<tr>
<td>Tumor size (cm)</td>
</tr>
<tr>
<td>Multicentricity (+/−)</td>
</tr>
<tr>
<td>Lymphovascular invasion (+/−)</td>
</tr>
<tr>
<td>Extrathyroidal extension (+/−)</td>
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<tr>
<td>Central metastasis (+/−)</td>
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<td>Lateral metastasis (+/−)</td>
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</table>

Table 2. The relationship of the clinicopathological factors with a TSH level of 2.5 (mIU/L)

<table>
<thead>
<tr>
<th>TSH &lt;2.5 (mIU/L)</th>
<th>TSH &gt;2.5 (mIU/L)</th>
<th>p</th>
<th>Odds ratio</th>
<th>95% confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extrathyroidal extension</td>
<td>24/66 (36.4%)</td>
<td>14/23 (60.9%)</td>
<td>0.410</td>
<td>2.722</td>
</tr>
<tr>
<td>Lateral metastasis</td>
<td>8/66 (12.1%)</td>
<td>3/23 (13.0%)</td>
<td>1.000</td>
<td>3.111</td>
</tr>
<tr>
<td>Tumor size (cm)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–2</td>
<td>52/66 (78.8%)</td>
<td>17/23 (73.9%)</td>
<td>0.528</td>
<td></td>
</tr>
<tr>
<td>2–4</td>
<td>12/66 (18.2%)</td>
<td>4/23 (17.4%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;4</td>
<td>2/66 (3.0%)</td>
<td>2/23 (18.0%)</td>
<td></td>
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</tr>
<tr>
<td>Multicentricity</td>
<td>26/66 (39.4%)</td>
<td>14/23 (60.9%)</td>
<td>0.075</td>
<td>2.393</td>
</tr>
<tr>
<td>Lymphovascular invasion</td>
<td>22/66 (33.3%)</td>
<td>14/23 (60.9%)</td>
<td>0.020</td>
<td>3.111</td>
</tr>
<tr>
<td>Central metastasis</td>
<td>11/66 (16.7%)</td>
<td>10/23 (43.5%)</td>
<td>0.009</td>
<td>3.846</td>
</tr>
</tbody>
</table>

Discussion

The idea of “higher levels of TSH is related with more aggressive DTC” is widely accepted in the literature [4–16]. Tumor aggressivity is thought to be related with the potential of metastasis to the lymph nodes primarily to the central neck area. However, the power of radiological imaging for the identification of central neck metastases in preoperative evaluation is limited [19].

To manage DTC and to propose the prognosis of the patients following treatment, clinicians have been working to find more factors and markers. In addition, the relationship of TSH with DTC has always been a challenging subject in the development, progress, and treatment
Ethics Committee approval: Ethics Committee approval was received for this study from the Ethics Committee of Istanbul Health Sciences University Şişli Hamidiye Etfal Training and Research Hospital.

Informed Consent: Informed consent was obtained from the patients who participated in this study.

Peer review: Externally peer-reviewed.


Conflict of Interest: The authors declared no conflicts of interest.

Financial Disclosure: The authors declare that this study has received no financial support.

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