

Relationship Between Thyroid-Stimulating Hormone Levels and Prognosis in Patients with Pituitary Thyrotropin-Secreting Adenomas: Post-print

Authors: Yu Nansheng

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Abstract

Objective: To analyze the relationship between thyroid-stimulating hormone (TSH) levels and prognosis in patients with pituitary thyrotropin adenoma.

Methods: Clinical data of 53 patients with pituitary thyrotropin adenoma were retrospectively collected. All patients received conventional treatment after examinations, and serum TSH levels were measured within 1 week before treatment. Patients were divided into Group I (n=20, TSH<2.5 m U/L) and Group II (n=33, TSH 2.5 m U/L) based on TSH levels. Both groups underwent follow-up for at least 5 years (or until death), and their disease-free survival and overall survival were recorded.

Results: There were no statistically significant differences in gender, age, or tumor diameter between the two groups ($P>0.05$). However, the lymph node metastasis rate in Group II was higher than that in Group I (36.36% vs 10.00%, $P<0.05$), the proportion of TNM stage III-IV was higher than that in Group I (57.58% vs 25.00%, $P<0.05$), and pre-treatment triiodothyronine and thyroxine levels in Group II were both higher than those in Group I, with statistically significant differences ($P<0.05$). As of February 2017, the 5-year disease-free survival rate and overall survival rate in Group II were 48.48% and 63.64%, respectively, which were lower than those in Group I (80.00% and 90.00%), with statistically significant differences ($P<0.05$). Cox regression hazard model analysis of risk factors revealed that lymph node metastasis, TNM stage, and levels of triiodothyronine, thyroxine, and TSH were independent influencing factors for 5-year post-treatment survival in patients with pituitary thyrotropin adenoma ($P<0.05$).

Conclusion: Elevated TSH levels are associated with poor prognosis in patients with pituitary thyrotropin adenoma, and clinical measures should be actively

taken to regulate patients' TSH levels.

Full Text

Preamble

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Relationship between TSH Level and Prognosis in Patients with Thyrotropin-Secreting Pituitary Adenoma

YU Nansheng

The People' s Hospital of Raoping, Chaozhou, Guangdong 515700, China

Abstract

Objective To explore the relationship between thyroid stimulating hormone (TSH) level and the prognosis of patients with thyrotropin-secreting pituitary adenoma.

Methods The clinical data of 53 patients with thyrotropin-secreting pituitary adenoma were retrospectively analyzed. All patients received routine treatment after examination. Serum TSH levels were measured one week before treatment, and patients were divided into Group I (n=20, TSH < 2.5 mU/L) and Group II (n=33, TSH ≥ 2.5 mU/L) based on TSH levels. Both groups were followed up for at least 5 years (or until death), and their disease-free survival and overall survival were recorded.

Results There were no significant differences in gender, age, or tumor diameter between the two groups ($P > 0.05$). However, Group II had a significantly higher lymph node metastasis rate than Group I (36.36% vs. 10.00%, $P < 0.05$), and the proportion of TNM stage III-IV was significantly higher in Group II than in Group I (57.58% vs. 25.00%, $P < 0.05$). Additionally, pre-treatment levels of triiodothyronine (T3) and thyroxine (T4) were significantly higher in Group II than in Group I ($P < 0.05$). As of February 2017, the 5-year disease-free survival rate and overall survival rate in Group II were 48.48% and 63.64%, respectively, which were significantly lower than those in Group I (80.00% and 90.00%, $P < 0.05$). Cox regression risk model analysis identified lymph node metastasis, TNM stage, and levels of T3, T4, and TSH as independent factors influencing the 5-year survival rate after treatment in patients with thyrotropin-secreting pituitary adenoma ($P < 0.05$).

Conclusion High TSH levels are associated with poor prognosis in patients with thyrotropin-secreting pituitary adenoma. Clinicians should actively implement symptomatic measures to regulate TSH levels in these patients.

Keywords: thyroid stimulating hormone; hyperthyroidism; thyrotropin-secreting pituitary adenoma; survival; prognosis

Introduction

Thyrotropin-secreting pituitary adenoma (TSPA) is a rare endocrine disease that predominantly affects young and middle-aged women. The main clinical manifestations include neck masses, and prolonged stimulation by excessive TSH can significantly increase the risk of thyroid cancer. Therefore, timely diagnosis and treatment are crucial for improving patient outcomes. Patients may present with compressive symptoms when the mass is large, and the thyroid mass moves upward and downward with swallowing, causing a foreign body sensation. Most patients also experience symptoms such as dyspnea, hoarseness, pain, hemoptysis, and obvious manifestations of hyperthyroidism and secondary pituitary dysfunction [1-3]. Although the incidence of TSPA is low, it can severely affect patient survival. While current treatment protocols have become increasingly well-defined, primarily including long-acting somatostatin analogs and/or surgical resection and/or gamma knife therapy, and surgical outcomes are relatively reliable with fewer postoperative complications, the prediction of treatment efficacy and prognosis for TSPA remains in the exploratory stage [4], and relevant reports have small sample sizes [8]. Clinical analyses have demonstrated that somatostatin analogs help normalize thyroid function, but assessment of complete remission rates after pituitary tumor treatment remains insufficiently accurate [5]. This study primarily analyzes whether TSH levels can be used for prognostic estimation in TSPA patients. Compared with existing clinical studies monitoring endocrine indicators [6], this study uses TSH level as the main evaluation metric, and all selected patients had a follow-up period of at least 5 years, which is valuable for assessing prognosis.

Methods

1.1 Clinical Data

We retrospectively selected 53 patients with thyrotropin-secreting pituitary adenoma admitted to our hospital between January 2008 and March 2012. All patients presented with symptoms including dyspnea, hoarseness, pain, hemoptysis, neck mass, and foreign body sensation during swallowing. The cohort comprised 17 males and 36 females, aged 24-64 years (49.50 ± 9.53 years), with body weight ranging from 41-64 kg (57.00 ± 4.18 kg) and tumor diameter of 2.04 ± 0.44 cm.

Inclusion criteria: Age 19 and 65 years; clinical manifestations of thyrotoxicosis; diagnosis confirmed by X-ray, CT, and postoperative pathology; no prior radioactive iodine treatment at admission; elective surgery after examination; complete clinical and follow-up data; informed consent; approval from our hospital ethics committee.

Exclusion criteria: Cardiac, pulmonary, hepatic, splenic, or endocrine diseases or other comorbidities; secondary cardiovascular disease or chronic pain syndrome; prior radiotherapy or chemotherapy; concurrent thyroiditis; pre-treatment use of thyroid hormone preparations; use of hormone drugs or other

medications affecting stress response and analgesia within 3 months; history of hyperthyroidism or hypothyroidism; psychiatric disorders or communication difficulties; alcohol or drug abuse; known allergy to anesthetic drugs; pregnant or lactating women.

1.2 Grouping Method

All enrolled patients had 5 mL of fasting venous blood collected in the early morning within one week before surgery. After centrifugation at 3000 r/min for 10 minutes, the supernatant was collected. TSH levels were measured using an electrochemiluminescence detection kit according to the manufacturer's instructions. The normal range for TSH levels was 0.55-4.78 mIU/L [7]. The 53 patients were divided into two groups based on TSH level: Group I (n = 20, TSH < 2.5 mIU/L) and Group II (n = 33, TSH ≥ 2.5 mIU/L).

1.3 Analysis Indicators and Treatment

We collected demographic data, medical history, laboratory tests [triiodothyronine (T3), thyroxine (T4)], and disease severity (tumor size, lymph node metastasis, TNM stage) at admission. Both groups received the same treatment after admission, consisting of long-acting somatostatin analogs and/or surgical resection.

1.4 Follow-up

Patients were followed up for at least 5 years (or until death) through outpatient review, email, telephone, and WeChat. Disease-free survival and overall survival were recorded, with overall survival defined as the period from the end of treatment to patient death or the last follow-up.

1.5 Statistical Methods

SPSS 19.0 software was used for statistical analysis. Count data were expressed as rates and compared between groups using the χ^2 test. Measurement data were expressed as mean \pm standard deviation and compared using the t-test. Kaplan-Meier survival curves and multivariate Cox regression analysis were used to study prognostic factors. $P < 0.05$ was considered statistically significant.

Results

2.1 Comparison of Clinical and Pathological Data Between Groups

There were no significant differences in gender, age, or tumor diameter between the two groups ($P > 0.05$). However, Group II had a significantly higher lymph node metastasis rate than Group I (36.36% vs. 10.00%, $P < 0.05$), and the proportion of TNM stage III-IV was significantly higher in Group II than in Group I (57.58% vs. 25.00%, $P < 0.05$) (Table 1).

2.3 Comparison of Kaplan-Meier Survival Between Groups

Pre-treatment T3 and T4 levels were significantly higher in Group II than in Group I ($P < 0.05$) (Table 2). As of February 2017, the follow-up rate was 100% in both groups, with a median follow-up time of 40.5 months in Group I and 40.8 months in Group II. The 5-year disease-free survival rate and overall survival rate in Group II were 48.48% (16/33) and 63.64% (21/33), respectively, which were significantly lower than those in Group I (80.00% [16/20] and 90.00% [18/20]; $\chi^2 = 5.17, 4.45, P < 0.05$) (Figures 1-2).

2.4 Cox Regression Analysis of Prognosis in TSPA Patients

Using overall survival time as the dependent variable and gender, age, tumor diameter, lymph node metastasis, TNM stage, and levels of T3, T4, and TSH as independent variables, a Cox regression model was fitted. Cox regression risk model analysis identified lymph node metastasis, TNM stage, and levels of T3, T4, and TSH as independent factors influencing the 5-year survival rate after treatment in TSPA patients ($P < 0.05$) (Table 3).

[Figure 1: see original paper]

[Figure 2: see original paper]

Discussion

The preferred treatment for thyrotropin-secreting pituitary adenoma is transsphenoidal pituitary adenoma resection, supplemented with appropriate drug therapy. Although clinical efficacy is typically evaluated by measuring thyroid function, assessing imaging changes in primary lesions, and monitoring postoperative complications, there is currently no unified standard for evaluating surgical efficacy of TSPA domestically or internationally. Furthermore, some patients may experience postoperative recurrence, which affects prognosis. Therefore, scholars believe that long-term postoperative follow-up is necessary for TSPA patients, and identifying laboratory indicators with high sensitivity for prognosis prediction is of great significance [9-10].

TSH is a thyroid growth factor secreted by the anterior pituitary that participates in cell growth and development, inhibits secretion of tumor necrosis factors, and plays an important role in promoting thyroid follicular epithelial cell proliferation and thyroid hormone synthesis and release [11-12]. TSH levels can reflect the severity of thyroid disease, especially in patients with papillary thyroid cancer who show significantly increased TSH expression [13]. TSH is also significantly correlated with thyroid hyperplasia and postoperative recurrence of nodular goiter [14]. This study analyzed the clinical data of 53 TSPA patients, measuring serum TSH levels within one week before surgery and dividing them into Groups I and II based on TSH levels. Group II had a significantly higher lymph node metastasis rate and a significantly higher proportion of TNM stage III-IV than Group I, and pre-treatment T3 and T4 levels were significantly

higher in Group II. These results suggest that TSH levels are closely related to lymph node metastasis and TNM stage in TSPA patients, consistent with the aforementioned reports. T3 and T4 are correlated with TSH levels, as their synthesis and secretion primarily depend on TSH, which promotes thyroid growth [15]. Current reports have also confirmed from a genetic perspective that T3, T4, and TSH levels are all involved in the pathogenesis of thyroid disease [16].

All patients in this study received surgical treatment supplemented with somatostatin analog therapy. Foreign studies have reported that preoperative use of somatostatin analogs can regulate preoperative thyroid function in TSPA patients to some extent and help reduce the volume of invasive tumors, thereby decreasing surgical difficulty [17-18]. After treatment, all 53 patients were followed up for 5 years to understand the prognosis of patients with different TSH levels. The results showed that as of February 2017, the 5-year disease-free survival rate and overall survival rate in Group II were significantly lower than those in Group I, suggesting that patients with higher TSH levels had lower 5-year disease-free and overall survival rates and poorer prognosis. Some studies have suggested that TSH levels are important in postoperative follow-up of TSPA patients and can predict and observe adenoma recurrence and progression [19,21], but these studies did not include patient prognosis in their analysis. This study's Cox regression risk model analysis identified lymph node metastasis, TNM stage, and levels of T3, T4, and TSH as independent factors influencing the 5-year postoperative survival rate in TSPA patients, indicating that high TSH levels can predict poor postoperative prognosis. The report by Li et al. [20] confirmed that high TSH levels are an independent factor for poor prognosis in differentiated thyroid cancer, which is consistent with our conclusion. Therefore, clinicians should pay attention to risk factors affecting the prognosis of TSPA patients and implement active, targeted preventive measures, especially regulating TSH levels, to improve patient outcomes.

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