Cellular and Molecular Biology

Journal homepage: www.cellmolbiol.org

Diagnostic and prognostic value of combined detection of serum Tg, IFN - γ and TgAb in thyroid adenoma

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ARTICLE INFO

Original paper

Article history:
Received: July 25, 2021
Accepted: October 23, 2021
Published: December 15, 2021

Keywords:
Thyroglobulin; interferon-γ; thyroglobulin antibody; thyroid adenoma; diagnosis; prognosis

ABSTRACT

This study aimed to explore the value of combined detection of serum thyroglobulin (Tg), interferon - γ (IFN - γ) and thyroglobulin antibody (TgAb) in the diagnosis and prognosis of thyroid adenoma (TA). For this purpose, 100 patients with TA in our hospital from January 2017 to December 2020 were selected as the observation group, and they were divided into good prognosis group (83 cases) and poor prognosis group (17 cases) according to the surgical treatment; another 50 healthy people who received physical examination in our hospital. The levels of serum Tg, IFN - γ and TgAb in each group were detected and compared; the diagnostic and prognostic value of combined detection of serum Tg, IFN - γ and TgAb in thyroid adenoma were analyzed. Results showed that compared with the control group, the levels of Tg and TgAb in the observation group were significantly increased, and the levels of IFN - γ were significantly decreased ($P < 0.05$); compared with the poor prognosis group, the levels of Tg and TgAb in the good prognosis group were significantly decreased, and the levels of IFN - γ were significantly increased ($P < 0.05$); The area under curve (AUC) of the combined detection of serum Tg, IFN-γ and TgAb for TA diagnosis and prognosis assessment was significantly higher than the value detected by a single indicator. In general, the combined detection of serum Tg, IFN - γ and TgAb has high diagnostic and prognostic value for TA, and has high clinical reference value.

DOI: http://dx.doi.org/10.14715/cmb/2021.67.5.39

Introduction

Thyroid adenoma (TA), as a common benign tumor of the thyroid, mainly occurs in thyroid follicular cells, mostly single, no tenderness, clear boundary, tough and with complete outer capsule (1). TA is more common in women under 40 years old, and its incidence is on the rise (2). TA grows slowly and develops into functional autonomous TA with the development of the disease, which causes hyperthyroidism and poses a certain threat to patients' quality of life and health (3, 4). Long-term clinical practice shows that early diagnosis and treatment is of great significance to improve the quality of life of TA patients. Most of the early TA patients have no significant clinical manifestations. With the gradual enlargement of the tumor, common symptoms such as dysphagia and dyspnea may be presented after the compression of the surrounding tissues, which are easily ignored and subsequently affect the clinical diagnosis and treatment. Currently, ultrasound, computed tomography (CT) and other imaging methods are mainly used in clinical diagnosis of TA patients. Although they have high safety, low cost and easy operation, they are easily affected by image resolution and characteristics, resulting in missed diagnosis and misdiagnosis (5-7). Therefore, it is necessary to find other more efficient diagnostic methods. In recent years, it has been found that thyroglobulin (Tg), interferon-γ (IFN-γ), thyroglobulin antibody, TgAb plays an important role in the occurrence and development of thyroid diseases (8, 9). However, few studies have explored its role in the progression of TA, which is worthy of further study. Therefore, this study mainly explored the diagnostic and prognostic value of serum Tg, IFN-γ and TgAb combined detection for TA, aiming to

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provide more reference ideas for the clinical diagnosis and treatment of TA.

Materials and methods

General Information

A total of 100 TA patients admitted to our hospital from January 2017 to December 2020 were selected as the observation group, and all patients received surgical treatment. The prognostic score criteria developed by the European Cancer Research and Treatment Group were used for calculation: age, Gender, the female score was 0, the male score was 12; Transfer: 15 points for transfer 1, 15* N points for transfer N; Infiltration, infiltration is 10 points, no infiltration is 0 points; For tissue type, 0 for papillary carcinoma, 45 for undifferentiated carcinoma and 10 for follicular carcinoma. The cumulative value of the above indexes ≥65 was classified as poor prognosis, and the cumulative value < 65 was classified as good prognosis.

After treatment, according to the prognosis score, TA patients were divided into the good prognosis group (n = 83) and the poor prognosis group (n = 17). Another 50 healthy people who underwent physical examination in our hospital during the same period were selected as the control group.

Inclusion and exclusion criteria

Inclusion criteria: After postoperative pathological diagnosis, all patients in the observation group were diagnosed with TA; Subjects who have not undergone thyroid surgery; Subjects with complete clinical data.

Exclusion criteria: Patients in the observation group had received relevant treatment before inclusion in the study; Subjects with diseases such as infection and immune system; Subjects with other tumor diseases; Subjects with other thyroid diseases; Pregnant or lactating women.

Detection Method

In the morning of the second day after the subjects were enrolled in the study, 3mL of fasting elbow venous blood was taken and placed in the EP tube. After standing at room temperature for 1 h, the serum was separated by centrifugation method and stored at -80°C for testing. The level of Tg was detected by radioimmunoassay. Serum IFN-γ levels were determined by an enzyme-linked immunosorbent assay (ELISA) kit provided by Hangzhou Huitu Biotechnology Co., LTD. Serum TgAb levels were measured by an automatic immune analyzer (Roche Cobas E602).

Observation Indicators

The levels of serum Tg, IFN-γ and TgAb in the observation group and the control group were compared. To analyze the diagnostic value of serum Tg, IFN-γ and TgAb in TA; The levels of serum Tg, IFN-γ and TgAb in the observation group were compared between the good prognosis group and the bad prognosis group. The prognostic value of serum Tg, IFN-γ and TgAb was analyzed.

Statistical methods

SPSS 18.0 was used for statistical analysis. The measurement data were expressed as mean ± standard deviation (± S) and tested by T. Enumeration data were expressed by example (n) or percentage (%) and tested by $\chi 2$. The comparison between multiple groups was tested by the F value. The diagnostic and prognostic value of serum Tg, IFN-γ and TgAb in TA were evaluated by the receiver Operator characteristic (ROC) curve. $P<0.05$ indicated a statistically significant difference.

Results and discussion

Comparison of general data in each group

There were 83 patients in the good TA prognosis group, including 21 males (25.30%) and 62 females (74.70%). There were 17 patients in the TA poor prognosis group, including 4 males (23.53%) and 13 females (76.47%). There were 13 males (26.00%) and 37 females (74.00%) in the control group, and there was no significant difference in gender among the three groups (P=0.887). The mean age of patients in the good TA prognosis group was (35.94±2.67) years old, the mean age of patients in the poor TA prognosis group was (36.43±2.73) years old, and the mean age of patients in the control group was (36.29±2.65) years old. There was no significant difference in age among the three groups (P=0.708). The average BMI was 25.61±0.54 in the group with a good TA prognosis, 25.14±0.56 in the group with poor TA prognosis, and 25.30±0.49 in the control group. There

was no significant difference in BMI among the three groups (P=0.639). The average tumor diameter was (2.37±0.20) cm in patients with good TA prognosis and (2.44±0.22) cm in patients with poor TA prognosis, with no statistical significance (P=0.501). In the TA group with a good prognosis, 54 patients (65.06%) had follicular thyroid adenoma and 29 patients (34.94%) had papillary cystic thyroid adenoma. In the TA poor prognosis group, 11 patients (64.71%) had follicular thyroid adenoma and 6 patients (35.29%) had papillary cystic thyroid adenoma. The difference was not statistically significant (P=0.492), as shown in Table 1.

Table 1. Comparison of general information of each group

General data		Good prognosis group (n=83)	Poor prognosis group (n=17)	Control group (n=50)	F/χ^2	*P*
Gender [n (%)]	Male	21 (25.30)	4 (23.53)	13 (26.00)	0.023	0.887
	Female	62 (74.70)	13 (76.47)	37 (74.00)		
Average age (year)		35.94±2.67	36.43±2.73	36.29±2.65	0.372	0.708
Average BMI (kg/m^2)		25.61±0.54	25.14±0.56	25.30±0.49	0.459	0.639
Mean tumor diameter (cm)		2.37±0.20	2.44±0.22	-	0.454	0.501
TA type [n (%)]	Funicular adenoma of the thyroid	54 (65.06)	11 (64.71)	-	0.473	0.492
	Papillary cystic adenoma of the thyroid	29 (34.94)	6 (35.29)	-		

Comparison of serum Tg, IFN-γ and TgAb levels between observation group and control group

Compared with the control group (28.21±1.03), the Tg level in the observation group (54.52±2.68) was significantly increased, and the difference was statistically significant (t=7.592, P=0.005). Compared with the control group (52.12±5.67), the level of TgAb in the observation group (126.84±12.80) was significantly increased, the difference was statistically significant (t=9.892, P=0.000). Compared with the control group (3.26±0.71), the level of IFN-γ in the observation group (1.67±0.74) was significantly lower (t=5.018, P=0.033), as shown in Figure 1 and Table 2.

Table 2. Comparison of serum Tg, IFN - γ and TgAb levels between the observation group and the control group (x̄±s)

Indicators	Observation group (n=100)	Control group (n=50)	*t*	*P*
Tg (ng/mL)	54.52±2.68	28.21±1.03	7.592	0.005
IFN-γ (ug/L)	1.67±0.74	3.26±0.71	5.018	0.033
TgAb (U/mL)	126.84±12.80	52.12±5.67	9.892	0.000

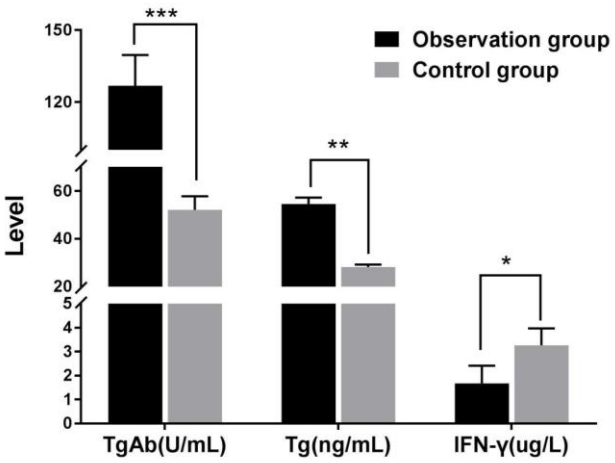

Figure 1. Comparison of serum Tg, IFN - γ and TgAb levels between the observation group and the control group
Note: Compared with the good prognosis group, **P*<0.05, ***P*<0.01, ****P*<0.001

Analysis of the diagnostic value of serum Tg, IFN-γ and TgAb combined detection for TA

Analysis of the diagnostic value of serum Tg, IFN-γ and TgAb alone and in combination in the control group and the observation group, the AUC of serum Tg level were 0.772 (95%CI: 0.687 ~ 0.858), the sensitivity was 0.800, the specificity was 0.683, the Yuden index was 0.483, and the optimal limit value was 50.38 (ng/mL). The AUC of serum IFN-γ level was 0.787 (95%CI: 0.706-0.867), the sensitivity was 0.783, the specificity was 0.717, the Yoden index was 0.500, and the optimal cut-off value was 16.94 (ug/L). The AUC of serum TgAb level was 0.839 (95%CI: 0.770-0.907), the sensitivity was 0.883, the specificity was 0.633, the Yoden index was 0.516, and the optimal limit value was 98.27 (U/mL). The AUC of serum Tg, IFN-γ and TgAb combined detection was 0.945 (95%CI: 0.905 ~ 0.984), the sensitivity was 0.867, the specificity was 0.917, and the Yoden index was 0.784, as shown in Figure 2 and Table 3.

Table 3. The value of combined detection of serum Tg, IFN - γ and TgAb in the diagnosis of TA

Indicators	Optimum limit value	Sensitivity	Specificity	Youden index	AUC	95%*CI*
Tg	50.38 (ng/mL)	0.800	0.683	0.483	0.772	0.687～0.858
IFN-γ	16.94 (ug/L)	0.783	0.717	0.500	0.787	0.706～0.867
TgAb	98.27 (U/mL)	0.883	0.633	0.516	0.839	0.770～0.907
The joint detection	-	0.867	0.917	0.784	0.945	0.905～0.984

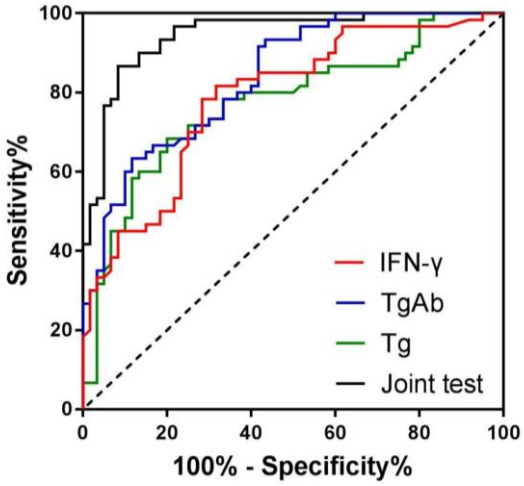

Figure 2. ROC curve of serum Tg, IFN-γ and TgAb alone or in combination in the diagnosis of TA

Comparison of serum Tg, IFN-γ and TgAb levels between the group with good prognosis and the group with poor prognosis

The Tg level in the poor prognosis group was significantly higher than that in the good prognosis group (41.65±2.27) (69.26±3.12), the difference was statistically significant (t=7.631, P=0.003). Compared with the good prognosis group (2.85±0.82), the level of IFN-γ in the poor prognosis group (1.20±0.54) was significantly lower (t=7.021, P=0.007). Compared with the TgAb level of the good prognosis group (77.60±8.21), the TgAb level of the poor prognosis group (156.27±10.61) was significantly higher, and the difference was statistically significant (t=9.936, P=0.000), as shown in Figure 3 and Table 4.

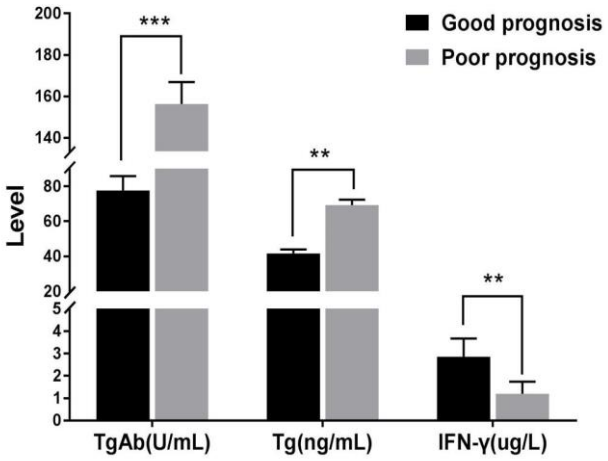

Figure 3. Comparison of serum Tg, IFN - γ and TgAb levels in the observation group with good prognosis and poor prognosis. Note: Compared with the good prognosis group, *P<0.05, **P<0.01, ***P<0.001

Table 4. Comparison of serum Tg, IFN - γ and TgAb levels in the observation group with good prognosis and poor prognosis

indicators	Good prognosis group (n=83)	Poor prognosis group (n=17)	*t*	*P*
Tg（ng/mL）	41.65±2.27	69.26±3.12	7.631	0.003
IFN-γ（ug/L）	2.85±0.82	1.20±0.54	7.021	0.007
TgAb（U/mL）	77.60±8.21	156.27±10.61	9.936	0.000

Analysis of the value of the combined detection of serum Tg, IFN-γ and TgAb in evaluating the good and bad prognosis of TA

To observe the diagnostic value of serum Tg, IFN-γ and TgAb alone and in combination in patients with good and poor TA prognosis. The AUC of serum Tg level was 0.747 (95%CI: 0.659 ~ 0.835), the sensitivity was 0.817, the specificity was 0.600, the Jorden index was 0.417, and the optimal limit value was 45.29 (ng/mL). The AUC of serum IFN-γ level was 0.738 (95%CI: 0.648-0.827), the sensitivity was 0.783, the specificity was 0.683, the Jorden index was 0.466, and the optimal cut-off value was 18.67 (ug/L). The AUC of serum TgAb level was 0.735 (95%CI: 0.647 ~ 0.824), the sensitivity was 0.500, the specificity was 0.917, the Yoden index was 0.417, and the optimal cut-off value was 123.15 (U/mL). The AUC of serum Tg, IFN-γ and TgAb combined detection was 0.847 (95%CI: 0.780-0.915), the sensitivity was 0.817, the specificity was 0.767, and the Yoden index was 0.584, as shown in Figure 4 and Table 5.

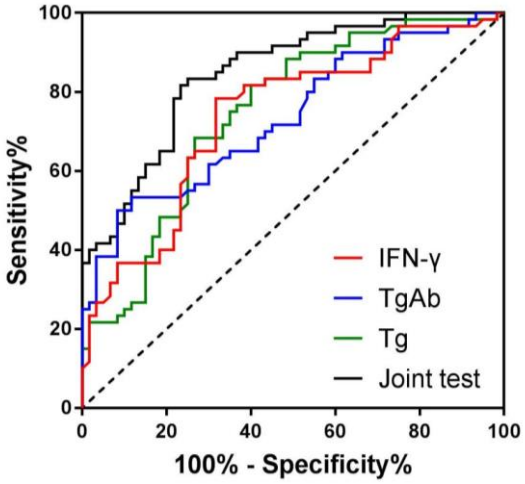

Figure 4. Table 5 ROC curve of serum Tg, IFN-γ and TgAb alone and in combination in the diagnosis of TA with good prognosis and poor prognosis

Table 5. Analysis of the prognostic value of combined detection of serum Tg, IFN - γ and TgAb in TA

Indicators	Optimum limit value	Sensitivity	Specificity	Youden index	AUC	95%*CI*
Tg	45.29 (ng/mL)	0.817	0.600	0.417	0.747	0.659～0.835
IFN-γ	18.67 (ug/L)	0.783	0.683	0.466	0.738	0.648～0.827
TgAb	123.15 (U/mL)	0.500	0.917	0.417	0.735	0.647～0.824
The joint detection	-	0.817	0.767	0.584	0.847	0.780～0.915

The clinical pathogenesis of TA is not completely clear, but relevant studies show that it may be closely related to radiation exposure, genetics, gender, thyroid-stimulating hormone stimulation, etc., with a high incidence in clinical practice, affecting the quality of life of human beings (10). If TA does not receive timely diagnosis and treatment, it may cause malignant transformation of tumor and hyperthyroidism, which increases the difficulty of clinical treatment (11, 12). As the best diagnostic method of TA, needle aspiration cytology has high accuracy, but it also has certain trauma. It is also affected by the operator's technical level and patient compliance, which in turn affects the diagnostic results (13-15). Serum markers are increasingly favored by clinical diagnosis and prognostic judgment. Tg, IFN-γ and TgAb are serum markers closely related to thyroid diseases (16, 17), but there are few studies on their combined detection value in TA diagnosis and prognostic analysis.

A number of studies (18-20) have found that Tg and TgAb levels in patients with thyroid cancer are effectively reduced after effective treatment, while the high expression level of IFN-γ suggests a poor prognosis in patients with thyroid cancer. In this study, the levels of serum Tg and TgAb in the observation group were abnormally higher than those in the control group, while the levels of IFN-γ were abnormally lower. Moreover, the range of changes in the observation group was more obvious in the group with poor prognosis, which was basically consistent with the results of Liu Xiaojie and Jiang Wen, indicating that the levels of serum Tg, IFN-γ and TgAb had significant changes after TA. And the worse the prognosis of patients, the changes of each index level are more significant. Serum Tg, as the main form of iodine stored in the thyroid gland, is a glycoprotein complex synthesized by the follicular epithelial cells of the body's thyroid gland. The content of Tg in normal human serum is very low, and it is also regulated by thyroid-stimulating hormone. Once thyroid diseases such as thyroid cancer, high-function adenoma and goiter occur, their expression level will be significantly increased and can be used as markers for the occurrence and development of thyroid diseases (21). As a common specific marker in thyroid autoimmunity, TgAb is an autoimmune antibody produced against Tg, which consists of immunoglobulins G1 (IgG1), IgG2 and IgG4. TgAb is not only a specific marker of thyroid disease, but also an initial marker of the occurrence of thyroid disease, through which patients' disease changes can be understood, and the higher the TgAb level, the worse the patient's condition (22, 23). IFN-γ is an inflammatory factor involved in a variety of cellular responses, which has antiviral, anti-tumor and immunomodulatory effects in clinical practice. IFN-γ also promotes the expression of compatible class antigens on thyroid cells and plays an important role in the production of specific thyroid antibodies such as TgAb by enhancing the ability of dendritic cells and macrophages to present the body's antigens (24, 25). Combined with the above results, it is indicated that serum Tg, IFN-γ and TgAb are closely related to the occurrence, development and prognosis of TA, suggesting that the clinical diagnosis of TA and prognosis of patients can be determined by detecting its level.

Fadime et al. (26) showed that serum Tg can not only effectively diagnose thyroid cancer, but also predict lymph node metastasis. Rakib et al. (27) showed that detection of TgAb level could differentiate benign and malignant thyroid nodules. In this study, serum Tg, IFN-γ and TgAb have certain diagnostic and prognostic values for TA, which is basically consistent with the results of Fadime and Rakib studies. However, single index detection has certain limitations, so a combination of multiple indicators is considered. In this study, the sensitivity, specificity and AUC of the combined detection of serum Tg, IFN-γ and TgAb for the diagnosis and prognosis assessment of TA were significantly higher than that of the single indicator, suggesting that the diagnostic rate of TA diagnosis and prognosis assessment can be improved by the combined detection of serum Tg, IFN-γ and TgAb. This has

important clinical reference value for clinical diagnosis and treatment of TA.

The limitation of this study lies in the small sample size, which may make the serum Tg, IFN-γ and TgAb values obtained in the study deviate from the actual values to some extent. Therefore, it is necessary to expand the sample size for further research verification, so as to provide a more reliable basis for clinical diagnosis, treatment and prognosis assessment of TA.

In conclusion, serum Tg, IFN-γ and TgAb levels have significantly changed in TA patients, which can effectively diagnose TA and evaluate its prognosis. The combined detection of the three has higher diagnostic and evaluation value and is worthy of clinical reference.

Acknowledgments

None.

Interest conflict

The authors declare no conflict of interest.

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