TgAb’s Change Trend and Degree of Decline Has Good Prognostic Value for Preoperative TgAb-Positive DTC Patients: A Retrospective Study in Southwest China

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Abstract

Purpose

Antithyroglobulin antibody (TgAb) is a potential tumor marker for the detection of recurrence of DTC, but there are not sufficient data supporting its application in clinical work. Our study aimed at describing change trend of TgAb after surgery and finding the relationship between this trend and clinical outcome of DTC.

Methods

We reviewed clinical data of 583 patients initially diagnosed with thyroid malignancy and underwent total thyroidectomy (TTx) in our hospital in 2016. Finally, 21 preoperative TgAb-positive DTC patients with persistent disease were included in Group A, and 37 preoperative TgAb-positive DTC patients survived without disease were included in Group B. Various clinical indicators and TgAbs at different timepoints were compared between two groups.

Results

In all 538 patients, 21.27% had preoperative TgAb positive (>115IU/mL), of which 16.94% survived with disease persistence/recurrence. Tumor, lymph node classification, and preoperative TgAb were significantly higher in Group A than B (P<0.05). TgAb of 23.81% patients in Group A became negative, and 89.19% in B. Compared with Group B, change trend of TgAb of Group A was more inclined stable or rising after surgery. Of patients with descending TgAb in Group A, their declines at first follow-up (40.75% vs 79.77%), the first year (76.67% vs 88.01%), the second year (80.00% vs 91.72%) after surgery were significantly lower than Group B (P<0.05). And the best cut-off values of three declines of TgAb for predicting clinical outcome were 43.32%, 72.81% and 84.36% respectively. Patients' clinical outcome was significantly associated with tumor classification T1a (OR=145.661, 95%CI: 2.462-8619.550) and TgAb decline at first follow-up (OR=158.858, 95%CI: 7.440-3392.024).

Conclusions

For preoperative TgAb-positive DTC patients, stable or rising trend of TgAb after surgery or TgAb decline less than 43.43% before the RRA or 6 months after surgery may predict disease persistence/recurrence.

Introduction

Thyroid cancer is currently the fifth most common cancer diagnosis in women. By the year 2030, it is estimated that it will be the second leading cancer diagnosis in women and the ninth leading cancer diagnosis in men[1]. Differentiated thyroid cancer (DTC) accounts the vast majority of thyroid cancer, mainly including papillary thyroid cancer (PTC) and follicular thyroid cancer (FTC). The prognosis of DTC patients is good, however, instances of persistent or recurrent disease like local lymph node metastasis are not uncommon, thus long-time observation after surgery of DTC patients is necessary. In the follow-
up of DTC patients, thyroglobulin (Tg) is the most sensitive and specific tumor marker for the early detection of recurrence\[^2\]. But antithyroglobulin antibody (TgAb) has potential interference with Tg assay especially immunometric assay (IMA) by forming Tg-TgAb complex, so simultaneous measurement of TgAb is essential\[^3\].

In the follow-up of DTC, the greatest challenge is patients with serum Tg-IMA concentrations suggestive of tumor absence in whom it is not possible to ensure whether this finding indicates complete remission or underestimated Tg due to the interference of TgAb\[^4\]. Many studies focus on the improvement of Tg detection technologies, like liquid chromatography/tandem mass spectrometry and radioimmunoassay, but the former may cause false-negative in many patients with structural disease\[^5\-^7\]; the latter is not suitable for clinical large-scale applications and may cause false-positive.

Nowadays, Tg measurement is widely performed by second-generation IMA. On the one hand, interference of detectable TgAb is inevitable, on the other hand, there is no better assays for the moment. Theoretically, the body produces TgAb due to the expression of Tg. For DTC patients underwent total thyroidectomy (TTx) and radioiodine ablation (RRA), there should be no residual thyroid tissue in the body under normal condition, thus TgAb should ideally be undetectable. We are therefore justified in holding that the behavior of TgAb may be a predictor of disease persistent/recurrent.

Though there are some researches focusing on the relationship between TgAb and clinical outcome of DTC, the current literatures don’t provide sufficient data for giving evidence-based answer to many questions arising in the care of TgAb-positive DTC patients\[^8\]. The general conclusion is that a reduction >50% in TgAb concentration compared to that detected before RRA associated with a low risk of disease persistent or recurrent\[^9\,^10\]. However, the 50% of TgAb decline was established empirically, not statistically. Our study calculated declines of TgAb at every follow-up timepoint for each subject, aiming at describing long-time dynamic change trend of TgAb and finding the relationship between this trend and clinical outcome.

**Materials And Methods**

**Patients**

This was a retrospective study approved by the Ethics Committee of West China Hospital of Sichuan University. We reviewed clinical data of 583 patients who were initially diagnosed with thyroid malignancy and underwent TTx in our hospital in 2016. According to their preoperative TgAb levels, 583 patients were divided into two groups: 1) 459 patients (78.73%) whose preoperative TgAb were negative (<115 IU/mL); and 2) 124 patients (21.27%) whose preoperative TgAb were positive (\(\geq 115\) IU/mL). According to clinical outcomes, 124 patients with positive TgAb were divided into two groups: 1) 103 patients (83.06%) survived without a disease; and 2) 21 patients (16.94%) survived with persistent/recurrent disease. Disease persistence/recurrence was defined as (meeting any of the following): 1) imaging examinations (neck ultrasonography, CT and MRI), diagnostic whole-body scan or
pathological examination suggested the persistence/recurrence of disease; 2) the level of basal serum Tg ≥ 0.2ng/mL, and TgAb was negative; 3) TgAb was positive and kept rising or remained unchanged over 1 year. Disease-free was defined not compliant with anyone above. Of 103 patients survived without disease, we screened 37 patients as controls following these rules: 1) follow-up time on record more than 5 years; 2) with the complete clinical data and had regular follow-up; and 3) with comparable age and sex composition to the disease-persistent group. See Figure 1 for the flowchart.

Methods

We collected information on patient age and sex, preoperative neck ultrasonographic and fine-needle aspiration (FNA) cytology reports, preoperative serological indexes (including thyroid stimulating hormone (TSH), free triiodothyronine (FT3), free thyroxin (FT4), thyroglobulin antibody (TgAb), thyroid peroxidase antibody (TPOAb)), surgical details, intraoperative or postoperative pathological results. First follow-up was conducted before the first RRA or 6 months (2 patients did not have radiotherapy) after surgery, and next follow-up was at least once a year. In addition, we collected follow-up information on imaging examinations (neck ultrasonography, CT and MRI), diagnostic whole-body scan, pathological examination and serological indexes.

Treatment and follow-up

All patients chosen in our study underwent TTx in our hospital, and neck lymph node dissections were performed according to preoperative imaging studies, the levels of serological indicators, and intraoperative morphological appearance. In Group A, 2 patients didn't receive RRA, 15 patients received one RRA, 3 patients twice, and 1 patient three times. In Group B, 34 patients received one RRA, 2 patients twice, and 1 patient three times. In Group A, 7 patients were detected for disease persistence/recurrence by imaging examinations, 6 patients by pathological examination, 4 patients by diagnostic whole-body scan, 3 patients by serum Tg levels ≥ 0.2ng/mL and keeping rising, and 1 patient by serum TgAb level keeping positive and rising for 2 years.

Laboratory analysis

Serum thyroid-related indicators measurements (including TSH, FT3, FT4, TgAb and TPOAb) were performed using electroluminescent method. Detection kits and instruments (cobas e 601 and cobas e 801 modules) were purchased from Roche Diagnostics GmbH. Scopes of detection for TSH, FT3, FT4, Tg, TgAb and TPOAb were 0.005-100μIU/mL, 0.6-50pmol/L, 0.5-100pmol/L, 0.04-500ng/mL, 10-4000IU/mL, 9-600IU/mL.

Statistical analysis

All continuous variables were tested for a normal distribution by the Kolmogorov–Smirnov (K-S) normality test. Then, normally distributed variables were expressed as the mean ± standard deviation (M±SD), and skewed variables were expressed as the median (the minimum value, the maximum value). The differences between the two groups were examined by unpaired two-tailed Student’s t-tests and
Mann-Whitney U-tests for normally and nonnormally distributed parameters, respectively. Categorical variables were compared by the chi-square test. Receiver operating characteristic (ROC) curves were used to evaluate the prediction effect of TgAb on clinical outcome. Binary logistics regression was used to analyze the risk factors for the persistence/recurrence of disease. P values of <0.05 were considered to be statistically significant. All statistical analyses were performed using SPSS 25.0.

Results

Patient clinic data and comparison

Patient clinic data are displayed in Table 1. The staging criteria for lymph node metastasis and tumor classification were according to the eighth edition of the American Joint Committee on Cancer (AJCC) TNM staging system. The risk of recurrence class was according to American Thyroid Association (ATA) risk stratification. Tumor, lymph node classification, and preoperative TgAb level were significantly higher in Group A than B (P<0.05), and there were more patients in Group A than B having tumor capsular invasion. There were no statistical significant differences in times of RRA and ATA risk stratification (P>0.05).

Table 1 Patient clinic data and comparison
| characteristic                  | Group A     | Group B     | P Value |
|--------------------------------|-------------|-------------|---------|
| **n**                          | 21          | 37          |         |
| **Sex (%)**                    |             |             |         |
| Male                           | 6 (28.57)   | 7 (18.92)   |         |
| Female                         | 15 (71.43)  | 30 (81.08)  | 0.05    |
| **Age, y**                     | 40.00±2.43  | 38.78±1.97  | 0.05    |
| **Times of RRA (%)**           |             |             |         |
| 0                              | 2 (9.52)    | 0 (0)       |         |
| 1                              | 15 (71.43)  | 34 (91.89)  |         |
| 2                              | 3 (14.29)   | 2 (5.41)    |         |
| 3                              | 1 (4.76)    | 1 (2.70)    | 0.05    |
| **Tumor classification (%)**   |             |             |         |
| T1a                            | 2 (9.52)    | 16 (43.24)  |         |
| T1b                            | 4 (19.05)   | 5 (13.51)   |         |
| T2                             | 1 (4.76)    | 3 (8.11)    |         |
| T3                             | 8 (38.10)   | 9 (24.32)   |         |
| T4                             | 6 (28.57)   | 4 (10.81)   | 0.05    |
| **Tumor capsular invasion (%)**|             |             |         |
| No invasion                    | 11 (52.38)  | 29 (78.38)  |         |
| Invasion                       | 10 (47.62)  | 8 (21.62)   | 0.05    |
| **Lymph node classification (%)**|           |             |         |
| N0                             | 1 (4.76)    | 2 (5.41)    |         |
| N1a                            | 8 (38.10)   | 27 (72.97)  |         |
| N1b                            | 12 (57.14)  | 8 (21.62)   | 0.05    |
| **ATA risk stratification (%)**|             |             |         |
| Low                            | 2 (9.52)    | 3 (8.11)    |         |
| Intermediate                   | 9 (42.86)   | 26 (70.27)  |         |
| High                           | 10 (47.62)  | 8 (21.62)   | 0.05    |
| **Preoperative TgAb (IU/mL)**  | 725.90(162.60-4000) | 353.50(117.20-40000) | 0.05    |
Change trend of TgAb after surgery and comparison between two groups

In Group A, 5 (23.81%) patients’ TgAb became negative during the follow-up period, and in Group B 33 (89.19%) patients’ TgAb became negative. Compared with Group B, change trend of TgAb of Group A was more inclined stable or rising after surgery, seeing Table 2. At every time point of follow-up after surgery, declines of TgAb were calculated by \[ \frac{(\text{TgAb at every time point}) - (\text{preoperative TgAb})}{(\text{preoperative TgAb})} \], seeing Table 3. The first decline of TgAb was calculated before receiving the first RRA or 6 months after surgery (2 patients didn't have RRA). First follow-up, the first-year and the second-year decline of TgAb were significantly higher in Group B than A (P<0.05). There were no statistical significant differences in the third-year, fourth-year and fifth-year declines of TgAb (P>0.05). The rate of decline of TgAb in two groups were both slowing down during the entire follow-up period, and decline at first follow-up was the biggest, seeing Figure 2.

Table 2 Change trend of TgAb after surgery of two groups
### Change trend of TgAb after the surgery

|                        | Group A | Group B | P Value |
|------------------------|---------|---------|---------|
| N                      | 21      | 37      |         |
| **First follow-up (%)**|         |         |         |
| Decline                | 16 (76.19) | 35 (94.59) |         |
| Stable or rising       | 5 (23.81)   | 2 (5.41)  | 0.052   |
| **First year (%)**     |         |         |         |
| Decline                | 12a (57.14) | 37 (100) |         |
| Stable or rising       | 4 (19.05)    | 0 (0)    | 0.05    |
| **Second year (%)**    |         |         |         |
| Decline                | 11b (52.38) | 37 (100) |         |
| Stable or rising       | 4 (19.05)    | 0 (0)    | 0.05    |
| **Third year (%)**     |         |         |         |
| Decline                | 10c (47.62) | 37 (100) |         |
| Stable or rising       | 4 (19.05)    | 0 (0)    | 0.05    |
| **Fourth year (%)**    |         |         |         |
| Decline                | 6d (28.57)  | 37 (100) |         |
| Stable or rising       | 5 (23.81)    | 0 (0)    | 0.05    |
| **Fifth year (%)**     |         |         |         |
| Decline                | 6e (28.57)  | 37 (100) |         |
| Stable or rising       | 2 (9.52)     | 0 (0)    | 0.05    |

* Five people reached the follow-up end point.
* Six people reached the follow-up end point.
* Seven people reached the follow-up end point.
* Ten people reached the follow-up end point.
* Thirteen people reached the follow-up end point.

**Table 3 Comparison of degrees of declines of TgAb after surgery**
### Table 3 Comparison of degrees of declines of TgAb after surgery

| Degrees of declines | First follow-up | First year | Second year |
|---------------------|----------------|------------|-------------|
| **Group A**         | 40.75%         | 76.67%     | 80.00%      |
|                     | (8.23%-94.65%) | (11.02%-98.62%) | (55.56%-99.53%) |
| **Group B**         | 79.77%         | 88.01%     | 91.72%      |
|                     | (9.30%-97.55%) | (13.31%-98.49%) | (26.78%-99.13%) |
| **P Value**         | ≈0.05          | ≈0.05      | ≈0.05       |

### Prediction efficacy of declines of TgAb on clinical outcome

To evaluate the prediction value of TgAb's declines on clinical outcome of DTC, ROC curves were generated, seeing **Figure 3**. The AUC of first follow-up, first-year and second-year declines of TgAb were 0.749, 0.675 and 0.724 respectively, and there were no statistical significant differences in prediction efficacy of these three declines, seeing **Table 4**. When the Youden index had a maximum value, the cut-off values of these three declines were 43.32%, 72.81% and 84.36% respectively.

### Table 4 Prediction efficacy of declines of TgAb on clinical outcome

|                   | First follow-up | First-year decline | Second-year decline | P Value |
|-------------------|-----------------|--------------------|---------------------|---------|
| **AUC**           | 0.762           | 0.678              | 0.708               | ≈0.05   |
| **S. E**          | 0.077           | 0.106              | 0.103               |         |
| **95% CI**        | 0.612-0.912     | 0.471-0.886        | 0.507-0.911         |         |
| **Cut-off**       | 43.32%          | 72.81%             | 84.36%              |         |
| **Sensitivity**   | 91.40%          | 89.20%             | 83.80%              |         |
| **Specificity**   | 56.20%          | 50%                | 36.40%              |         |

Results of binary logistic regression
Binary logistic regression analysis showed that patients’ clinical outcome was significantly associated with tumor classification T1a (OR=145.661, 95%CI: 2.462-8619.550) and TgAb decline at first follow-up (OR=158.858, 95%CI: 7.440-3392.024). The preoperative TgAb level, tumor capsular invasion and lymph node classification were not significantly associated with patients’ clinical outcome in binary logistic regression. Seeing Table 5.

### Table 5 Results of binary logistic regression

| Variables                     | Group            | B    | SE   | Wald  | P      | OR       | OR 95%CI     |
|-------------------------------|------------------|------|------|-------|--------|----------|--------------|
| **Tumor classification**      |                  |      |      |       |        |          |              |
| T1b                           | T1a              | 4.981| 2.082| 5.725 | .017   | 145.661  | 2.462-8619.550|
| T2                            | T1b              | 4.058| 2.203| 3.395 | .065   | 57.864   | .772-4337.365 |
| T3                            | T2               | 1.679| 1.502| 1.249 | .264   | 5.359    | .282-101.772  |
| T4                            | T3               | .739 | 2.131| .120  | .729   | 2.093    | .032-136.346  |
| **Tumor capsular invasion**   | No invasion      |      |      |       |        |          |              |
| invasion                      | invasion         | 1.857| 1.844| 1.015 | .314   | 6.404    | .173-237.580  |
| **Lymph node classification** | N0               |      |      |       |        |          |              |
| N1a                           | N0               | -.955| 2.503| .146  | .703   | .385     | .003-51.981  |
| N1b                           | N1a              | .835 | 2.463| .115  | .735   | 2.304    | .018-287.975  |
| **TgAb decline**              | ≥43.43%          |      |      |       |        |          |              |
| at first follow-up            | ≥43.43%          | 5.068| 1.562| 10.529| .001   | 158.858  | 7.440-3392.024|
| Preoperative TgAb             | .001             |      |      | 2.479 | .115   | 1.001    | 1.000-1.001  |

### Discussion

Usually, TgAb is a serum biomarker for the diagnosis and follow-up of thyroid autoimmune diseases. However, due to following three characteristics, TgAb has been more valued as a prognostic indicator for DTC patients: 1) about 20%~30% of patients with DTC have TgAb positive on initial postoperative
assessment\textsuperscript{[11, 12]}; 2) the presence of TgAb compromises the authenticity of Tg, and it’s recommended that measuring the level of TgAb when Tg measurement; 3) ideally, for DTC patients underwent TTx and RRA, TgAb level should decrease to undetectable without stimulation of Tg. Many cross-sectional studies focus on relationship between the level of TgAb and DTC, but the prognostic significance of TgAb status (positive/negative) is less clear\textsuperscript{[13]}. Compared to observing TgAb at the single time-point, TgAb trends appear to have more clinical utility as a surrogate tumor marker in the surveillance of TgAb-positive DTC patients\textsuperscript{[14]}, for that the trend of TgAb is reported to be associated with higher tumor metabolism\textsuperscript{[15]}. Most existing literatures concluded that an increase in TgAb can indicate disease presence\textsuperscript{[16-18]}, and some literatures empirically used a reduction of 50% of TgAb to group subjects, finding the reduction >50% can represent a good prognostic\textsuperscript{[19]}. Based on these studies, our study described overall TgAb change trends after surgery for preoperative TgAb-positive DTC patients and compared different change trends between patients with different clinical outcomes, aiming at further elucidating the prognostic value of TgAb.

In this study, we retrospectively reviewed clinical data of 583 DTC patients underwent TTx in our hospital, and 21.27% had preoperative TgAb positive. Over a median follow-up of 53.2 months, TgAb-positive patients were divided into two groups according to clinical outcomes, and 16.94% survived with disease persistence/recurrence. The preoperative Tg level was significantly higher in patients with disease persistence/recurrence than without, but in multifactor logistic regression analysis the preoperative Tg was not a risk factor for disease persistence/recurrence, which consistent with the conclusion of McLeod, Donald S. A.\textsuperscript{[20]} Just as Gorges, R reported, the development and course of TgAb in DTC patients cannot be predicted by initial TgAb levels\textsuperscript{[21]}, we next focused on the change of TgAb in whole follow-up. The first decline of TgAb was calculated before receiving the first RRA or 6 months after surgery (2 patients didn’t have RRA), and subsequently declines were calculated once a year. Throughout the whole follow-up, TgAb of disease-free patients showed a downward trend overall and 89.19% became negative before the end of follow-up; and TgAb of disease-persistent/recurrent patients were more inclined stable or rising and only 23.81% became negative, consistent with the general view that TgAb persistent/increasing trends were associated with compromised DTC prognosis\textsuperscript{[13, 22]}. Though TgAb of disease-persistent/recurrent patients were more inclined stable or rising, TgAb of half patients in Group A showed a downward trend. But declines of TgAb at first follow-up (40.75%), the first year (76.67%) and the second year (80.00%) after surgery were significant lower in Group A than B, which suggested that not only the change trend of TgAb but also the degree of TgAb’s decline could predict clinical outcome. ROC curves were drawn and declines at first follow-up, the first year and the second year after surgery were found to have good predictive efficacy for the clinical outcome, and the cut-offs were 43.32%, 72.81% and 84.36% respectively. Trimboli, P reported TgAb's significant drop (36.4%) 6-12 months after RRA could be considered a favorable factor\textsuperscript{[23]}. The reasons for the difference may be different calculation method of the decline of TgAb and different human race of subjects. Finally, tumor classification, tumor capsular invasion, lymph node classification, TgAb decline at first follow-up and preoperative TgAb level were brought into binary logistic regression analysis, and tumor classification
more than T1a and TgAb decline less than 43.43% before RRA or 6 months after surgery were risk factors of disease persistence/recurrence.

Our study has great significance for preoperative TgAb-positive DTC patients, for that TgAb is a routine test for DTC patients, which is more available and cheaper than image examinations. By observing the trend and degree of TgAb's decline, early metastasis and recurrence of the disease can be found in time, thus improving patients’ prognosis. Considering data on this area lacking especially in Asia, we hope our work could provide more evidence and help for clinical work. The limitation in our study is that using a reduction 43.3% of TgAb to predict the disease outcome has 91.4% sensitivity but only 56.20% specificity, which means some patients with TgAb decline less than 43.43% before the RRA or 6 months after surgery may not have disease persistent/recurrent. Under this circumstance, more image examinations like I-131 WBS and 18-fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT) may be needed to identify whether disease has recurred.

**Conclusion**

For preoperative TgAb-positive DTC patients, stable or rising trend of TgAb after surgery or TgAb decline less than 43.43% before the RRA or 6 months after surgery may predict disease persistence/recurrence.

**Declarations**

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**Availability of data and materials:** The datasets used and analyzed in this study are available from the corresponding author on reasonable request.

**Code availability:** Not applicable.

**Authors' contributions:** All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Qianhui, Liu. The first draft of the manuscript was written by Qianhui, Liu and Mengting, Yin, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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**Consent to participate:** Not applicable

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References

[1] MD B R H. 2015 American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer: What is new and what has changed? %J Cancer [J]. 2017, 123(3).

[2] R H B, K A E, C B K, et al. 2015 American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer: The American Thyroid Association Guidelines Task Force on Thyroid Nodules and Differentiated Thyroid Cancer. %J Thyroid : official journal of the American Thyroid Association [J]. 2016, 26(1).

[3] HJIYIANAKIS P, MUNDY J, HARMER C. Thyroglobulin antibodies in differentiated thyroid cancer [J]. Clin Oncol, 1999, 11(4): 240-4.

[4] WESLLEY R P, SOUZA C M C, GABRIELA F M. Follow-up of patients with thyroid cancer and antithyroglobulin antibodies: a review for clinicians. %J Endocrine-related cancer [J]. 2021, 28(4).

[5] NETZEL B C, GREBE S K G, LEON B G C, et al. Thyroglobulin (Tg) Testing Revisited: Tg Assays, TgAb Assays, and Correlation of Results With Clinical Outcomes %J The Journal of Clinical Endocrinology & Metabolism [J]. 2015, 100(8).

[6] UMAL A, KYLE P, LEIGHA S, et al. Thyroglobulin Liquid Chromatography-Tandem Mass Spectrometry Has a Low Sensitivity for Detecting Structural Disease in Patients with Antithyroglobulin Antibodies. %J Thyroid : official journal of the American Thyroid Association [J]. 2017, 27(1).

[7] LEILA G, S K T, D N C C, et al. The role of a new polyclonal competitive thyroglobulin assay in the follow-up of patients with differentiated thyroid cancer with structural disease but low levels of serum thyroglobulin by immunometric and LC-MS/MS methods. %J Endocrine [J]. 2020.

[8] A V F, MARKUS L, CRISTINA C, et al. Implications of thyroglobulin antibody positivity in patients with differentiated thyroid cancer: a clinical position statement. %J Thyroid : official journal of the American Thyroid Association [J]. 2013, 23(10).

[9] WESLLEY R P, MARINA C, FRANCO M G, et al. Comparison of Antithyroglobulin Antibody Concentrations Before and After Ablation with 131I as a Predictor of Structural Disease in Differentiated Thyroid Carcinoma Patients with Undetectable Basal Thyroglobulin and Negative Neck Ultrasonography. %J Thyroid : official journal of the American Thyroid Association [J]. 2016, 26(4).

[10] KIM W G, YOON J H, KIM W B, et al. Change of Serum Antithyroglobulin Antibody Levels Is Useful for Prediction of Clinical Recurrence in Thyroglobulin-Negative Patients with Differentiated Thyroid Carcinoma %J The Journal of Clinical Endocrinology & Metabolism [J]. 2008, 93(12).

[11] L D B, A V D H-S A N, J S W, et al. Clinical Applicability of Low Levels of Thyroglobulin Autoantibodies as Cutoff Point for Thyroglobulin Autoantibody Positivity. %J Thyroid : official journal of
the American Thyroid Association [J]. 2019, 29(1).

[12] PIERPAOLO T, VALENTINA Z, MAURO I, et al. Thyroglobulin autoantibodies before radioiodine ablation predict differentiated thyroid cancer outcome. %J Clinical chemistry and laboratory medicine [J]. 2017, 55(12).

[13] GIANOUKAKIS A G. Thyroglobulin antibody status and differentiated thyroid cancer: what does it mean for prognosis and surveillance? [J]. Curr Opin Oncol, 2015, 27(1): 26-32.

[14] G G A. Thyroglobulin antibody status and differentiated thyroid cancer: what does it mean for prognosis and surveillance? %J Current opinion in oncology [J]. 2015, 27(1).

[15] MORBELLI S, FERRARAZZO G, POMPOSELLI E, et al. Relationship between circulating anti-thyroglobulin antibodies (TgAb) and tumor metabolism in patients with differentiated thyroid cancer (DTC): prognostic implications [J]. J Endocrinol Invest, 2017, 40(4): 417-24.

[16] MATRONE A, LATROFA F, TORREGROSSA L, et al. Changing Trend of Thyroglobulin Antibodies in Patients With Differentiated Thyroid Cancer Treated With Total Thyroidectomy Without I-131 Ablation [J]. Thyroid, 2018, 28(7): 871-9.

[17] ZAVALA L F, BARRA M I, OLMOS R, et al. In properly selected patients with differentiated thyroid cancer, antithyroglobulin antibodies decline after thyroidectomy and their sole presence should not be an indication for radioiodine ablation [J]. Arch Endocrinol Metab, 2019, 63(3): 293-9.

[18] SEO J H, LEE S W, AHN B C, et al. Recurrence detection in differentiated thyroid cancer patients with elevated serum level of antithyroglobulin antibody: special emphasis on using 18F-FDG PET/CT [J]. Clin Endocrinol, 2010, 72(4): 558-63.

[19] REVERTER J L, ROSAS-ALLENDE I, PUIG-JOVE C, et al. Prognostic Significance of Thyroglobulin Antibodies in Differentiated Thyroid Cancer [J]. J Thyroid Res, 2020, 2020: 6.

[20] MCLEOD D S A, COOPER D S, LADENSON P W, et al. Prognosis of Differentiated Thyroid Cancer in Relation to Serum Thyrotropin and Thyroglobulin Antibody Status at Time of Diagnosis [J]. Thyroid, 2014, 24(1): 35-42.

[21] GORGES R, MANIECKI M, JCNTZEN W, et al. Development and clinical impact of thyroglobulin antibodies in patients with differentiated thyroid carcinoma during the first 3 years after thyroidectomy [J]. Eur J Endocrinol, 2005, 153(1): 49-55.

[22] LEE Z J O, ESLICK G D, EDIRIMANNE S. Investigating Antithyroglobulin Antibody As a Prognostic Marker for Differentiated Thyroid Cancer: A Meta-Analysis and Systematic Review [J]. Thyroid, 2020, 30(11): 1601-12.
[23] TRIMBOLI P, ZILIOLI V, IMPERIALI M, et al. Thyroglobulin autoantibodies before radioiodine ablation predict differentiated thyroid cancer outcome [J]. Clin Chem Lab Med, 2017, 55(12): 1995-2001.

**Figures**

**Figure 1**

Flowchart of including study subjects.
Figure 2

Change trends of TgAb after surgery in two groups

Figure 3

First follow-up
First-year decline
Second-year decline
ROC curves of declines of TgAb