

Stimulated Thyroglobulin 5 Years after Initial Treatment Detects Recurrence in 5.4% of Patients Despite a Thyroglobulin on T₄ <1 ng/ml

Rosario PW, Furtado MS, Fiho AF, Lacerda RX, Calsolari MR. Value of repeat stimulated thyroglobulin testing in patients with differentiated thyroid carcinoma considered to be free of disease in the first year after ablation. Thyroid. December 16, 2011 [Epub ahead of print]. doi: 10.1089/thy.2011.0214.

Background

It is not clear when or if TSH-stimulated thyroglobulin (Tg) testing should be repeated in patients with differentiated thyroid carcinoma who are thought to be disease-free after the initial therapy. This study evaluated the utility of repeat TSH-stimulated Tg testing in patients considered to be free of disease 6 to 12 months after the initial thyroid ablation who also had a Tg <1 ng/ml while on TSH-suppressing doses of levothyroxine.

Methods and Results

Medical records were reviewed for 307 subjects with differentiated thyroid cancer who had evidence of complete resection of tumor after total thyroidectomy and ablation with 1.1 to 5.5 GBg (\sim 30 to \sim 150 mCi) ¹³¹I (RAI) with a posttherapy whole-body scan (WBS) showing no distant metastases. This group was considered to be disease-free 6 to 12 months after ablation when they had a TSH-stimulated Tg <2 ng/ml (negative thyroglobulin antibody [TgAb] level) and a negative diagnostic RAI WBS. Patients were excluded if they had evidence of distant metastases, TSH-stimulated Tg >2 ng/ml at 6 to 12 months after ablation, positive TgAb, or apparent disease (n = 58). At this institution, after an initial treatment with total thyroidectomy and RAI ablation all patients routinely had TSH-stimulated Tg for confirmation of the absence of disease (Tg <2 ng/ml).This cohort of patients continued to have an annual exam with neck ultrasonography, Tg and TgAb measurements. If the TSH-stimulated Tg was >2 ng/ml, neck ultrasonography; CT scans of the neck, chest, and mediastinum; and a 99mTc-methoxyisobutyl isonitrile (MIBI) scan were obtained. If the TSH-stimulated Tg was >10 ng/ml in a patient with apparent disease, then an empirical dose of 3.7 GBq (100 mCi) $^{131}\mathrm{I}$ was administered and a posttherapy scan was performed.

There were 203 patients who met the inclusion criterion of being disease-free (Tg on $T_4 < 1$ ng/ml, negative TgAb, and no clinical evidence of tumor recurrence) 5 years after initial therapy. Ten patients were excluded because of a Tg on $T_4 > 1$ ng/ml, positive TgAb, or clinical tumor recurrence. Evaluation 54 to 64 months after initial therapy showed that 192 patients (94.6%) had hypothyroid-stimulated Tg <2 ng/ml and 188 of these patients had a stimulated Tg <1 ng/ml. During the subsequent follow-up, for a mean of 102 months, there were no new cases of tumor recurrence in this subgroup. Eleven (5.4%) of the 203 patients had a stimulated Tg >2 ng/ml. Of these patients 3 had nodal metastases found on neck ultrasound, 5 had metastases (2 neck nodes,1 mediastinal node, and 2 pulmonary metastases) found on other imaging methods (CT scan, 99mTc-MIBI, or posttherapy RAI WBS). In the remaining 3 patients, no metastases were found, and stimulated Tg continued to be mildly elevated, at >2ng/ml (2.3, 3.5, and 5 ng/ml).

Conclusions

There were 11 (5.4%) patients initially considered to be disease-free in whom a stimulated Tg >2 ng/ml had developed when they were evaluated between 54 and 64 months after initial treatment. The entire cohort was followed for a mean of 102 months. Metastases were located in 8 of these 11 patients. This recurrent disease was not associated with sex, age, or original AJCC staging of the tumor. All the patients had identical initial treatment with total thyroidectomy and RAI ablation. None of the patients with a low stimulated Tg level at 54 to 64 months had tumor recurrence over a mean of 102 months of follow-up.

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Stimulated Thyroglobulin 5 Years after Initial Treatment Detects Recurrence in 5.4% of Patients Despite a Thyroglobulin on $T_4 < 1 \text{ Ng/MI}$

ANALYSIS AND COMMENTARY • • • • • •

The 2009 American Thyroid Association Guideline for Thyroid Nodules and Cancer suggests using both the TNM AJCC/UICC staging plus risk factors to completely assess risk for death and persistence/recurrence of the tumor (1). In addition, there has been the suggestion that patients should be "restaged" periodically, taking into account absence or progression of disease (2). The advantages of this study are that the patients had identical initial treatment with total thyroidectomy and RAI ablation and were carefully evaluated for recurrence over a long time (mean, 8.5 years). This careful follow-up likely resulted in a higher detection of recurrence (5.4%) as compared with the literature (3). In this cohort who initially at 6 to 2 months were considered to be free of disease (negative neck ultrasound, stimulated Tg <2 ng/ml, and negative RAI WBS), half of the recurrences were found clinically and half were found only after hypothyroid-stimulated Tg testing. This study supports

repeat TSH-stimulated Tg testing 5 years after ablation in patients thought to be disease-free 6 to 12 months after treatment despite a Tg on $T_4 < 1 \text{ ng}/$ ml and negative TgAb tests. Other investigators have suggested, with a negative predictive value of 100%, a second negative stimulated Tg in patients initially believed to be disease-free (4). It is an important result that a negative predictive value of 100% was achieved for patients followed for a mean of 102 months when a negative stimulated Tg was found at 5 years. This result suggests that no further stimulated Tg tests are necessary. My conclusion is that it is reasonable to repeat a stimulated Tg at 5 years even if the patient is considered to be disease-free. If the Tg is >2 ng/ml, this would allow for early detection of recurrences and/or intensified follow-up for these patients while reducing or stopping follow-up of patients with a low stimulated Tg.

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