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MANAGEMENT OF GRAVES' HYPERTHYROIDISM IN PATIENTS WITH ORBITOPATHY

Bartalena L. **The dilemma of how to manage Graves' hyperthyroidism in patients with associated orbitopathy**. J Clin Endocrinol Metab. doi:10.1210/jc.2010-2329

SUMMARY

BACKGROUND

Some of the thyrotropin (TSH) receptor antibodies that develop in susceptible individuals can promote thyroid growth, vascularity, and hormone secretion and cause Graves' hyperthyroidism. In orbital tissues from patients with active Graves' orbitopathy, the TSH receptor levels may be higher than in controls, but how TSH receptor antibodies may be related to the development of Graves' orbitopathy remains unclear. Orbitopathy remains clinically silent or is mild in most patients with Graves' disease, and the therapy chosen to treat hyperthyroidism rarely seems to affect their orbitopathy. However, controversy exists about the best way to treat hyperthyroidism in the minority of patients with Graves' disease whose orbitopathy becomes clinically problematic.

METHODS

The author reviewed 30 years of literature on how different approaches to treating Graves' hyperthy-roidism may affect associated Graves' orbitopathy.

RESULTS

Orbitopathy can appear while patients are euthyroid while taking antithyroid drugs. Hypothyroidism can affect the eyes, too, so patients being treated with antithyroid drugs need to have their thyroid hormone levels monitored frequently. (The TSH level may be misleading, since it can remain low for some time after serum triiodothyronine and thyroxine levels have fallen below normal). Furthermore, when antithyroid drug treatment is discontinued, hyperthyroidism recurs in about half of cases. Although radioiodine is a common and effective treatment for Graves' hyperthyroidism, randomized trials show that it does increase the risk of orbitopathy developing or becoming worse, as compared with antithyroid drug treatment. In one randomized trial, the risk of orbitopathy progressing after thyroidectomy was the same as after antithyroid drug therapy (1). The risk of orbitopathy developing or becoming worse is substantially increased in smokers. Radioiodine treatment, severe or recent onset of hyperthyroidism, persistently high TSH-binding inhibitory antibodies, and preexisting orbitopathy are also factors associated with an

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increased risk of progressive orbitopathy. Although high-dose glucocorticoids can cause serious side effects, they ameliorate the risk of orbitopathy after radioiodine treatment and also reduce the increased risk of orbitopathy in patients who smoke.

There is no consensus as to the best way to treat active inflammatory orbitopathy. Some prescribe low-dose oral glucocorticoids even for mild orbitopathy. For moderate-to-severe orbitopathy, close follow-up by a team of experienced ophthalmologists and endocrinologists is important, but the therapy chosen still remains a matter of "expert opinion." Oral or intravenous glucocorticoids are commonly used as the initial therapy, but surgery or orbital radiotherapy may be needed if florid inflammation shows no response after a few weeks. The concurrent hyperthyroidism in such cases is often treated with antithyroid drugs initially, while postponing any decision concerning ablative therapy (surgery or radioiodine) until active orbitopathy has been quiescent for 6 months or longer. Once orbitopathy appears to be stable, diplopia or disfiguring proptosis can be treated with reconstructive surgery. Another point of view, however, is that the thyroid should be ablated promptly after euthyroidism is achieved with antithyroid drugs, concomitant with treatment of the orbitopathy, and prompt thyroid ablation is indicated if the hyperthyroidism is not controlled with antithyroid drug therapy.

CONCLUSIONS

Objective randomized, clinical trials are needed for establishing the best way to treat hyperthyroidism in patients with active moderate-to-severe orbitopathy.

COMMENTARY

The natural history of Graves' hyperthyroidism and that of orbitopathy are quite variable, and the term active moderate-to-severe orbitopathy lacks specificity. Objective ways to assess the degree of edema, fibrosis, and the levels of specific inflammatory cells separately in each of the various orbital structures would be an important advance in determining what antithyroid therapy is best, as would finding epitope-specific antibodies that correlate with specific orbital responses.

— Stephen W. Spaulding, MD

Reference

1. Tallstedt L, Lundell G, Tørring O, et al. Occurrence of ophthalmopathy after treatment for Graves' hyperthyroidism. N Engl J Med 1992;326:1738.

BLOCK-REPLACEMENT TREATMENT OF HYPERTHYROIDISM MAY BE USEFUL IN GRAVES' ORBITOPATHY

Elbers L, Mourits M, and Wiersinga W. **Outcome of very long-term treatment with antithyroid drugs in Graves' hyperthyroidism associated with graves' orbitopathy.** Thyroid, December 29, 2011. doi: 10.1089/thy.2010.0181

SUMMARY

BACKGROUND

Antithyroid drugs are generally used to treat Graves' hyperthyroidism in one of two ways: 1) to completely block the synthesis of thyroid hormone while also replacing thyroid hormone, or 2) to titrate the dose of antithyroid drug to maintain just enough hormone synthesis to keep the patient euthyroid. Randomized trials of the titration approach have shown that if the drugs are discontinued after only 6 months, Graves' hyperthyroidism recurs in the following year more often than if drugs are continued for 12 months: continuing the drugs for more than 18 months is not more effective. These studies did not address how orbitopathy responded. Over the past 50 years, however, numerous uncontrolled retrospective studies have indicated that using antithyroid drug therapy for longer periods is associated with lower rates of recurrent hyperthyroidism. This perception is supported by the current retrospective study, which used the blocking/replacement approach for patients with moderate-to-severe orbitopathy until the orbitopathy needed no further treatment, which generally took at least 2 years.

METHODS

All 255 patients who had been referred to the Orbital Center of the Academic Medical Center in Amsterdam for Graves' orbitopathy between 1995 and 2005 were sent a questionnaire. Of these 255 patients, 114 returned the questionnaire: 28 were excluded because their local endocrinologist had changed the treatment method, 10 did not provide sufficient data, and 3 had not given informed consent, leaving 73 patients for the study. The patients were given a constant dose of antithyroid drug (generally, 30 mg of methimazole) plus thyroxine replacement, and the regimen was stopped only when no further medical and surgical treatment was required for Graves' ophthalmopathy other than eye lubricants (median treatment period, 3.5 years, range, 2 to 12). About 30% of patients remained active smokers at the time that the antithyroid regimen was discontinued. The majority of the patients had undergone orbital decompression surgery, almost half had undergone irradiation and eyelid surgery, about 45% had received glucocorticoids, and about 40% had undergone eye muscle surgery. Only about 10% had received none of these treatments for their orbitopathy.

RESULTS

Hyperthyroidism did not recur in 46 patients (63%) after medical treatment was stopped (mean follow-up, 51 months; range, 12 to 124). Of the 27 patients (37%) who did have recurrence of hyperthyroidism (median time to recurrence, 3 months; range, 1 to 65), 19 were then treated with radioactive iodine (^{131}I); in the remaining 8, antithyroid drug treatment was restarted. These 27 patients were subsequently followed for mean periods of 69 and 30 months, respectively. Two patients indicated on their questionnaires that they had some worsening of eye symptoms after they had stopped antithyroid drugs, although a review of their records did not substantiate physical worsening of their Graves' ophthalmopathy. Otherwise, there was no worsening of ophthalmopathy in any of the 73 patients, regardless of whether they were in the group that had a recurrence of Graves' hyperthyroidism (median follow-up, 63 months; range, 12 to 170) or not (median follow-up, 51 months; range, 12 to 124).

CONCLUSIONS

The recurrence rate of 37% is less than what has generally been reported in studies with shorter periods of antithyroid drug treatment and with shorter periods of follow-up. No differences in clinical or lab tests were detected between the group that had recurrent hyperthyroidism and the group in whom hyperthyroidism did not recur. No substantial worsening of Graves' orbitopathy was observed, even in the 19 patients whose recurrent hyperthyroidism was treated with ^{131}I.

COMMENTARY

None of the patients did, in fact, require further orbital therapy, which confirms the expertise of this group. Although patient questionnaires were initially used, the responses were confirmed by contacting the specialists treating the patients if the patients were no longer being followed at the Orbital Center. Nonetheless, only about a third of patients invited to participate were finally included. Some were excluded because their thyroid disease had been "prematurely" treated with radioactive iodine or thyroidectomy; presumably none of these cases was resistant to the antithyroid drug regimen. Despite these potential drawbacks to the study, several facts support the concept that prolonged antithyroid treatment can reduce recurrences: (1) Graves' disease will eventually burn out in many patients, (2) thyroid-stimulating immunoglobulin levels do tend to drop following treatment with antithyroid drugs (or surgery), (3) certain thionamides appear to have immunosuppressive properties, and (4) some of the risk factors for a relapse of Graves' hyperthyroidism are also associated with increased risk of progression of Graves' ophthalmopathy (e.g., smoking and goiter size). If more specific TSH receptor antibodies correlate consistently with the activity of orbitopathy (1), they could prove useful in determining when to perform reconstructive orbital surgery and/or discontinue antithyroid drug therapy.

— Stephen W. Spaulding, MD

REFERENCE

1. Lytton SD, Ponto KA, Kanitz M, et al. A novel thyroid stimulating immunoglobulin bioassay is a functional indicator of activity and severity of Graves' orbitopathy J Clin Endocrinol Metab 2010;95: 2123-31.

NORMAL PARATHYROID HORMONE LEVELS DO NOT EXCLUDE THE DIAGNOSIS OF HYPOPARATHYROIDISM AFTER THYROIDECTOMY

Promberger R, Ott J, Kober F, Karik M, Freissmuth M, Hermann M. **Normal parathyroid hormone levels do not exclude permanent hypoparathyroidism after thyroidectomy.** Thyroid. December 29, 2010 [Epub ahead of print].

SUMMARY

BACKGROUND

Permanent hypoparathyroidism is the most common complication after thyroid surgery and may occur in 4% of patients. The aim of this study was to analyze a series of patients with long-term hypocalcemia who had normal serum parathyroid hormone (PTH) concentrations.

METHODS

The authors evaluated eight patients who had normal PTH levels with subnormal serum calcium levels 2 months after thyroidectomy. Calcium metabolism and bone turnover markers were studied carefully at 2 months and 12 months after surgery.

RESULTS

There were seven women and one man, with a mean age of 54 years. Four patients had benign nodular goiter, three had thyroid cancer, and one (age 19) had Graves' disease. The patients with carcinoma had total thyroidectomy and the others had near-total thyroidectomy. The parathyroid glands were visualized during surgery, and in only one patient was there removal of two parathyroid glands for oncologic reasons. Seven of the eight patients had symptomatic hypocalcemia within 1 day after surgery and the other was symptomatic at 6 days. All were treated with long-term calcium therapy. Although PTH levels were initially low postoperatively, they rose progressively and were well within the normal range at 2 and 12 months after surgery. At 1 year, total calcium was slightly low in all eight patients and ionized calcium was low in six; all patients had normal magnesium and 25-hydroxyvitamin D levels.

CONCLUSIONS

In patients with persistently low calcium levels during long-term follow-up after thyroidectomy, even normal PTH values may represent an insufficient parathyroid response.

COMMENTARY

This report provides an excellent description of mild hypoparathyroidism in the presence of normal serum PTH in patients who have had a thyroidectomy resulting in damage to the parathyroid glands. The authors, who are surgeons, do not describe the management of the hypocalcemia in these patients. This job usually falls to the endocrinologist. I shall describe a similar case that illustrates the subtle abnormalities of mild postoperative hypocalcemia. The son of a medical colleague had a total thyroidectomy for a papillary thyroid cancer with resection of two parathyroid glands and implantation of one gland into the sterncleidomastoid muscles. He had severe transient symptomatic hypocalcemia postoperatively, despite PTH in the lower normal range, followed by calcium levels in the low-normal range after tapering and then discontinuing calcitriol and calcium supplementation while consuming generous amounts of milk over the next five years. His mother, an endocrinologist, noted that he was twitching when moving into his college dormitory. In retrospect, he related that he felt that he could not run as fast nor could he jump since his surgery. Reevaluation showed total serum calcium in the lower half of the normal range and normal PTH levels, but ionized calcium was frankly low. He was empirically started on calcitriol and calcium supplements with resolution of twitching and a great improvement in his running and jumping in basketball games. The lesson here is that post-thyroidectomy hypoparathyroidism may be subtle, with symptoms of hypocalcemia manifest only during metabolic stress, and that a normal serum PTH level in this context may be misleading.

— Jerome M. Hershman, MD

SERUM THYROGLOBULIN >2.5 NG/ML AFTER RECOMBINANT TSH PREDICTS RECURRENCE OF DIFFERENTIATED THYROID CARCINOMA

Kloos RT. **Thyroid cancer recurrence in patients clinically free of disease with undetectable or very low serum thyroglobulin values.** J Clin Endocrinol Metab 2010;95:5241-8. Epub September 15, 2010.

SUMMARY

BACKGROUND

The purpose of this study was to determine the utility of recombinant human thyrotropin (TSH)-stimulated thyroglobulin (rhTSH-Tg) for prediction of the recurrence of differentiated thyroid carcinoma.

METHODS

This is a follow-up study of a cohort of 107 patients with differentiated thyroid carcinoma first reported in 2002. Tumor pathology was papillary carcinoma in 80%, Hürthle-cell variant in 1%, tall-cell carcinoma in 2%, follicular carcinoma in 11%, and Hürthle-cell carcinoma in 6%. The patients were initially classified into three groups based on the rhTSH-Tg level: <0.5, 0.6 to 2.0, and >2.0 ng/ml. Patients were followed by conventional methods, including measurement of serum Tg while on thyroxine (T_4) therapy and neck ultrasonography. Patients with undetectable Tg levels underwent periodic rhTSH-Tg at a minimum of every 5 years. If Tg levels, whether stimulated or during T_4 therapy, rose above 0.5 ng/ml, various imaging studies were performed to detect recurrence.

RESULTS

Of the 60 patients with rhTSH-Tg levels <0.5 ng/ml, 2 had recurrent disease that was surgically resected, and 3 others converted to rhTSH-Tg levels of 0.6 to 2 ng/ml without detectable recurrence. Of the 19 patients in group with rhTSH-Tg levels of 0.6 to 2 ng/ml, 12 converted to rhTSH-Tg levels <0.5 ng/ml, 5 remained the same, and 2 had tumor recurrences that were treated. Of the 20 patients with rhTSH-Tg levels >2 ng/ml, 16 had tumor recurrences during follow-up.

CONCLUSIONS

An rhTSH-Tg level of >2.5 ng/ml predicts tumor recurrence with a sensitivity of 80%, but recurrent disease occurs in some patients with initial rhTSH-Tg levels <0.5 ng/ml.

COMMENTARY

This study provides additional data to emphasize the utility of measuring rhTSH-Tg levels to predict the recurrence of disease in patients with differentiated thyroid cancer. The results also show that 3% of those who would be predicted to have no recurrence based on rhTSH-Tg levels <0.5 ng/ml do indeed have recurrences of thyroid cancer. The report does not provide data on the pathology of these tumors that might also have predictive value, since follicular and Hürthle-cell and tall-cell papillary carcinomas are known to be more aggressive and recurrent (1). The report also shows that 7 additional patients in the group with rhTSH-Tg levels >2 ng/ml had recurrence after the first follow-up of this cohort in 2005 (2).

When patients with stage 1 thyroid cancer have an undetectable rhTSH-Tg levels during 9 to 12 months of follow-up after thyroidectomy, the ETA guidelines recommend that serum TSH levels should subsequently be maintained in the normal range (3). However, the 3% recurrence rate found in this study suggests to me that this is unwise. One advantage of allowing the serum TSH levels to be in the normal range, rather than suppressed to prevent recurrence, is that subsequent Tg measurements on replacement will be more sensitive for the detection of recurrence.

— Jerome M. Hershman, MD

References

1. Hundahl SA, Fleming ID, Fremgen AM, Menck HR. A National Cancer Data Base report on 53,856 cases of thyroid carcinoma treated in the U.S., 1985-1995. Cancer 1998;83:2638-48.

2. Kloos RT, Mazzaferri EL. A single recombinant human thyrotropin-stimulated serum thyroglobulin measurement predicts differentiated thyroid carcinoma metastases three to five years later. J Clin Endocrinol Metab 2005;90:5047-57. Epub June 21, 2005.

3. Pacini F, Schlumberger M, Dralle H, et al. European consensus for the management of patients with differentiated thyroid carcinoma of the follicular epithelium. Eur J Endocrinol 2006;154:787-803.

BRAF MUTATION IS POSITIVE IN A LOW PERCENTAGE OF CASES OF THE FOLLICULAR VARIANT OF PAPILLARY THYROID CANCER

Proietti A, Giannini R, Ugolini C, Miccoli M, Fontanini G, Di Coscio G, Romani R, Berti P, Miccoli P, Basolo F. **BRAF status of follicular variant of papillary thyroid carcinoma and its relationship to its clinical and cytological features.** Thyroid 2010;20:1263-70. Epub October 17, 2010.

SUMMARY

BACKGROUND AND METHODS

The follicular variant of papillary thyroid carcinoma (FVPTC) typically has a follicular pattern, and less than 1% of the tumor shows papillary formations. Yet these follicular cells have nuclear features of papillary thyroid carcinoma. The mutational status of the BRAF gene was evaluated in 187 FVPTCs diagnosed on histologic examination independently by three pathologists in Italy. Each patient had surgery after a fine-needle aspiration biopsy (FNAB) had been performed that had been classified by the British Thyroid Association Guidelines as inadequate (n = 19; Thy1), benign (n = 19; Thy2), follicular lesion/follicular lesion with atypia (n = 109; Thy3), suspicious for PTC (n = 20; Thy4), or malignant (n = 11; Thy5).

RESULTS

The BRAF mutational status (V600E, K600E, wt) correlated with the cytologic classification in 54.5% of malignant lesions, 27.6% of lesions suspicious for PTC, 12% of follicular lesions, and 9.3% of follicular lesions with atypia. The FNABs of the first 68 cases were examined for four cytologic features: nuclear grooves, intranuclear cytoplasmic inclusion bodies, number of cells per high-power field, and mean nuclear diameter. These cytologic findings were not associated with the BRAF mutation. BRAF mutations occurred in 16.6% of FVPTC, and most of these had suspicious or positive cytology on FNAB;. 30 cases showed a V600E mutation and 1 case had a K601E mutation. The BRAF mutations were not associated with any clinicopathological parameters, including age, sex, size of tumor, extrathyroidal extension, or lymph-node metastases. Although there was extrathyroidal extension in 24.5% of the BRAF tumors compared to 15.7% of the wild type BRAF tumors, this was not statistically significant.

CONCLUSIONS

Because BRAF is mutated in a low percentage of FVPTC and most of these mutated cases are suspicious or positive on fine-needle aspiration, analysis for BRAF is of limited value in the preoperative diagnosis of FVPTC.

COMMENTARY

FVPTC is a common variant of papillary thyroid carcinoma. The presence of this variant was hotly debated for many years. Dr. Austin Vickery, a leading thyroid cytopathology expert at the Massachusetts General Hospital, refused to acknowledge this subtype. Even today, the diagnosis can be difficult despite attempts to standardize morphologic characteristics of FVPTC or use molecular characterization. This difficulty was demonstrated when 10 expert thyroid pathologists evaluated 87 cases of FVPTC: only 39 % had a concordant diagnosis (1). The BRAF point mutation occurs in classic PTC with a frequency that varies from 29% to 83%. Furthermore, BRAF has been associated more with PTCs that have a papillary rather than the follicular pattern (2). Thus, it is not surprising that this study found BRAF mutations in only a small fraction of the FVPTC tumors. This study demonstrates that finding a BRAF mutation is seldom helpful in distinguishing benign from malignant lesions for FNABs read as "indeterminate" that result in a patient being sent to surgery for possible cancer. In fact, BRAF positivity in the FVPTC whose cytology was read as a "follicular lesion" or a "follicular lesion with atypia" was low, approximately 10%. The applicability of this data in the United States is not clear, as the cytologic interpretation in Italy may be different from what is standard in the United States. Of concern is that in this group of FVPTC, 10% had an

FNAB that indicated benign cytology. It is not indicated why these patients had a thyroidectomy. Further, 63% of the biopsies were reported as indeterminate or insufficient, a much higher percentage than that reported in the United States (3). Another limitation of this study is the lack of clinical correlation of tumors that showed metastatic spread of the FVPTC with the presence of the BRAF point mutation. BRAF testing of thyroid FNAB specimens may have a role in the preoperative risk stratification of PTCs, as several other studies have shown that the presence of BRAF mutation is strongly associated with extrathyroidal extension and lymph-node metastases with a poorer clinical prognosis (4,5).

— Stephanie L. Lee, MD

References

1. Lloyd RV, Erickson LA, Casey MB, et al. Observer variation in the diagnosis of follicular variant of papillary thyroid carcinoma. Am J Surg Pathol 2004;28:1336-40.

2. Adeniran AJ, Zhu Z, Gandhi M, et al. Correlation between genetic alterations and microscopic features, clinical manifestations, and prognostic characteristics of thyroid papillary carcinomas. Am J Surg Pathol 2006;30:216-22.

3. Yassa L, Cibas ES, Benson CB, et al. Long-term assessment of a multidisciplinary approach to thyroid nodule diagnostic evaluation. Cancer 2007;111:508-16.

4. Xing M, Clark D, Guan H, et al. BRAF mutation testing of thyroid fine-needle aspiration biopsy specimens for preoperative risk stratification in papillary thyroid cancer. J Clin Oncol 2009;27:2977-82. Epub May 4, 2009.

5. Xing M, Westra WH, Tufano RP, et al. BRAF mutation predicts a poorer clinical prognosis for papillary thyroid cancer. J Clin Endocrinol Metab 2005;90:6373-9. Epub September 20, 2005.

SURVIVAL IS SIMILAR IN FAMILIAL AND NONFAMILIAL NONMEDULLARY THYROID CANCER

Robenshtok E, Tzvetov G, Grozinsky-Glasberg S, Shraga-Slutzky I, Weinstein R, Lazar L, Serov S, Singer J, Hirsch D, Shimon I, Benbassat C. **Clinical characteristics and outcome of familial nonmedullary thyroid cancer: a retrospective controlled study.** Thyroid 2011;21:43-8. Epub October 18, 2010.

SUMMARY

BACKGROUND

Familial nonmedullary thyroid carcinoma (FNMTC) constitutes about 10% of differentiated thyroid cancer diagnosed worldwide. There is a difference of opinion in the literature as to whether the familial disorder is more aggressive than sporadic cancer and whether it is more likely to recur.

METHODS

A retrospective review of the patients in the Rabin Medical Center Thyroid Cancer Registry was performed for patients initially treated during the years 1973 to 2004. Cases were deemed familial if there were two or more first-degree relatives affected with histopathologic confirmation of thyroid cancer of follicular-cell origin.

RESULTS

The study compared 67 patients with FNMTC with 375 patients with sporadic nonmedullary thyroid cancer (SPNMTC) with regard to age, size of tumor, type of tumor, staging, treatment, and recurrence. Ninety percent of patients in each group had papillary thyroid cancer, the remainder being follicular. There were no differences between the groups in mean tumor size, multifocality, capsular invasion, lymph-node involvement, or distant metastases. Treatment regimens were similar, and mean follow-up was 8.5 years for both groups. There was no difference between the groups in recurrence, persistence, or new distant metastases. Disease-free survival was 80% in both groups. Although disease-free survival was better in those with three or more affected relatives (90%) than in those with two affected relatives (77%), the difference was not significant.

CONCLUSIONS

The results indicate that familial nonmedullary thyroid cancer is not more aggressive than sporadic nonmedullary thyroid cancer.

COMMENTARY

Some previous studies have suggested that familial nonmedullary thyroid cancer is more aggressive than the sporadic form, but other studies do not support this contention. A recent Japanese study of 273 patients with familial papillary thyroid cancer (1) reported that disease-free survival and cause-specific survival rates were similar to those with sporadic papillary carcinoma. However, because of a greater incidence of multicentricity in the familial form than in the sporadic condition (46% vs. 38%), they recommended total thyroidectomy for familial papillary thyroid cancer, a procedure usually not used in Japan for stage 1 disease.

The causes of FNMTC have not yet been identified, so there is no genetic screening for the disease in contrast with familial medullary thyroid cancer. When there are only two affected members, there is a distinct possibility that the condition is sporadic, but there is a 96% likelihood of the disease being genetic when there are three or more affected family members. Current studies on the genetics of FNMTC were reviewed recently by Khan et al. (2).

— Jerome M. Hershman MD

References

1. Ito Y, Kakudo K, Hirokawa M. Biological behavior and prognosis of familial papillary thyroid carcinoma. Surgery 2009;145:100-5.

2. Khan A, Smellie J, Nutting C, Harrington K, Newbold K. Familial nonmedullary thyroid cancer: a review of the genetics. Thyroid 2010;20:795-801.

RESPONSE TO INITIAL THERAPY REFINES THE ESTIMATED RISK OF RECURRENCE OF THYROID CANCER

Tuttle RM, Tala H, Shah J, Leboeuf R, Ghossein R, Gonen M, Brokhin M, Omry G, Fagin JA, Shaha A. **Estimating risk of recurrence in differentiated thyroid cancer after total thyroidectomy and radioactive iodine remnant ablation: using response to therapy variables to modify the initial risk estimates predicted by the new American Thyroid Association staging system.** Thyroid 2010;20:1341-9. Epub October 29, 2010.

SUMMARY

BACKGROUND

Staging systems for thyroid cancer are aimed mainly at predicting death, which is relatively rare, fortunately, in most forms of thyroid cancer. However, recurrence of the cancer is much more common. The ATA has developed a set of criteria to predict recurrence based on the findings at surgery, pathology, and the postablative radioiodine scan. The purpose of this clinical study was to evaluate the prediction for recurrence based on evaluation of clinical data at a 2-year follow-up.

METHODS

Of 710 eligible patients at the Memorial Sloan-Kettering Cancer Center initially treated from 1994 to 2004, a total of 588 had accurate clinical and pathologic information to allow for initial and 2-year risk stratification. All patients had undergone thyroidectomy and radioiodine remnant ablation. Patients with medullary or anaplastic cancer were excluded, as were those under the age of 18 years. The ATA low-risk category has no metastases, no invasion of local structures, removal of all macroscopic tumor, absence of aggressive histology, no vascular invasion, and no radioiodine (^{131}I) uptake outside the thyroid bed as seen on posttherapy scans. The intermediate-risk group had microscopic invasion outside the thyroid or cervical lymph-node metastases or positive uptake outside the thyroid as seen on the radioiodine scan or tumor with aggressive histology. The high-risk group had macroscopic tumor invasion or incomplete resection or distant metastases. The response at 6 to 24 months was categorized as excellent, acceptable, or incomplete based on suppressed and stimulated thyroglobulin levels <1 ng/ml, neck ultrasound, and imaging studies.

RESULTS

Initial stratification placed 23% of the patients into the ATA low-risk category, 49% into the intermediate–risk category, and 27% into the high-risk category (percentages do not sum to 100 because of rounding). Persistent or recurrent thyroid cancer was found in 3% of patients in the low-risk category, 21% in the intermediate–risk category, and 68% in the high-risk category. When patients were stratified based on the response to therapy during the first 2 years of follow-up, 34% had an excellent response, 20% had an acceptable response, and 46% had an incomplete response. The patients were then recategorized into the ATA categories. The likelihood of recurrence was then only 2% in the new low-risk category, 2% in the intermediate-risk category, and 14% in the high-risk category. An incomplete response to initial therapy increased the likelihood of recurrence to 13% in low–risk, 41% in intermediate-risk, and 79% in high-risk patients.

CONCLUSIONS

The data show that the recently proposed ATA categorization is effective for predicting the risk of recurrence. In addition, the assessment of response to the initial therapy can be used to further refine the prediction of recurrence.

COMMENTARY

There is a plethora of staging systems for thyroid cancer aimed mainly at predicting mortality (1,2). For treatment of typical patients, useful guidelines for predicting recurrence of the cancer are needed. This study makes a significant contribution to the management of thyroid cancer by showing how data that clinicians routinely obtain in follow-up can be useful for predicting the possibility of recurrence. It is likely that the patients referred to this tertiary-care center included a higher proportion of patients with aggressive disease than are seen in ordinary practice. I believe that this makes the data even more valuable because it shows the clinical course of patients with more advanced disease who are treated at a specialized center.

Of the patients in the high-risk category, 14% had no evidence of disease during follow-up, but unfortunately 86% of patients in this category had persistent or recurrent disease. Although the study does not describe the efficacy of various treatments, it is clear that many patients were moved to lower risk categories. Nevertheless, current therapeutic modalities are not optimally effective. For example, neck dissection for recurrence in cervical lymph nodes cures only about one-fourth of patients when strict criteria for cure are applied (3). Cure of metastatic disease by ^{131}I therapy is even less effective, although it is a time-honored tool (Schlumberger and colleagues [4]). Let's hope that the advances in the efficacy of therapy catch up with the advances in the prediction of recurrence.

— Jerome M. Hershman, MD

References

1. Dulgeroff AJ, Hershman JM. Medical therapy for differentiated thyroid carcinoma. Endocr Rev 1994;15:500-15.

2. Brierley JD, Panzarella T, Tsang RW, et al. A comparison of different staging systems predictability of patient outcome: thyroid carcinoma as an example. Cancer 1997;79:2414-23.

3. Al-Saif O, Farrar WB, Bloomston M, et al. Long-term efficacy of lymph node reoperation for persistent papillary thyroid cancer. J Clin Endocrinol Metab 2010;95:2187-94. Epub March 23, 2010.

4. Durante C, Haddy N, Baudin E, et al. Long-term outcome of 444 patients with distant metastases from papillary and follicular thyroid carcinoma: benefits and limits of radioiodine therapy. J Clin Endocrinol Metab 2006;91:2892-9. Epub May 9, 2006.

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COMMENTARY

Survey of Radioiodine Therapy Safety Practices Highlights the Need for User-Friendly Recommendations

Richard T. Kloos, M.D.[1–3]

Fetuses whose mothers are treated with radioiodine after approximately 10–12 weeks of pregnancy are at high risk of developing iatrogenic hypothyroidism (1). Other than this well-documented occurrence, there is no evidence of harm to others from radiation originating from patients treated with radioiodine. Given that radioiodine is concentrated in breast milk and radioiodine has been documented to be taken up by the thyroid in nursing newborns whose mothers were given diagnostic activities of radioiodine (2), discontinuing lactation before radioiodine therapy and avoiding breastfeeding after radioiodine treatment is justified despite the lack of a case report of infantile hypothyroidism ascribed to radioiodine ingestion from breastfeeding. Aside from circumstances relating to pregnancy and lactation, the harm that a radioiodine-treated patient could inflict upon another person while following common sense instructions appears to be low. Patients, who themselves receive a much higher dose of radiation because they ingest the full radioiodine treatment, suffer relatively few side effects. For the most part these occur in tissues that actively take up the radionuclide, and the adverse effects occur in a dose-dependent manner (3). This provides some reassurance that the small amount of radiation exposure to the public from those who receive radioiodine treatment is unlikely to cause harm, even if the treated patients ignore nearly all of the radiation safety instructions they receive. On the other hand, it is known that thyroidal exposure to higher levels of radiation, especially in children, can result in harm (4) and by extrapolation with a linear no-threshold dose–response relationship, one may assume that exposure to low levels of radiation might result in some harm. Thus, this theoretical possibility of increased harm at any increase of radiation exposure beyond background radiation, combined with no evidence of benefit of radiation exposure to the public, has led to the practice of keeping radiation exposure to others As Low As Reasonably Achievable (ALARA).

High levels of radiation exposure are dangerous. It has been estimated that half of the people receiving a dose to the whole body over a few minutes to a few hours of between 3500 and 5000 mSv would die within 30 days (multiple mSv by 100 to convert to mrem). Similarly, high-dose exposure (starting somewhere between 100 and 1000 mSv) over a relatively short period of time, is associated with the development of a number of malignancies. Conversely, the average yearly radiation exposure from natural sources to an individual in the United States is approximately 3 mSv. Radon gas accounts for two thirds of this exposure, while cosmic, terrestrial, and internal radiation account for the remainder. No adverse health effects have been demonstrated from these levels of natural radiation exposure. In addition, artificial sources of radiation from medical, commercial, and industrial activities contribute another 0.6 mSv, for a total average yearly radiation exposure of 3.6 mSv. Doses (in mSv) from common medical imaging procedures include the following: bitewing dental x-ray, 0.004; chest x-ray (posterior-anterior), 0.02; lateral lumbar spine x-ray, 0.3; mammography, 0.7; lung ventilation/perfusion scan, 1.5; barium swallow, 1.5; technetium-99m bone scan, 4.4; barium enema, 7; 2-deoxy-2[F-18]fluoro-D-glucose positron emission tomography scan, 7; chest or abdominal computed tomography scan, 8-10; and coronary angiogram, 5–16. A personalized annual radiation dose estimate can be calculated at the website http://www.epa.gov/radiation/understand/calculate.html.

Although radiation may cause cancers at high doses and dose rates, currently there are no data that unequivocally establish the occurrence of cancer following exposure to low doses or dose rates (e.g., below about 100 mSv). People living in areas with high levels of background radiation (>10 mSv per year) such as Denver, Colorado, have shown no adverse biological effects. Keep these millisievert values in mind as you read the next paragraph.

Effective May 29, 1997, and updated on July 29, 2009, the Nuclear Regulatory Commission (NRC) revised Federal Regulation 10 CFR 35.75, which permits NRC-licensed facilities to release a patient treated with radioiodine from their control if the total effective dose equivalent to any other individual from exposure to the released individual is not likely to exceed 5 mSv. Further, a licensee must provide the released individual, or the individual's parent or guardian, with instructions (including written instructions) on actions

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Editor-in-Chief's Note: This commentary was solicited by the Editor-in-Chief. Dr. Kloos was asked to provide a commentary based on his expertise and to indicate and reference, where appropriate, actions and positions of the ATA.

recommended to maintain doses to other individuals ALARA if the total effective dose equivalent to any other individual is likely to exceed 1 mSv. Several studies of the current practice have reported that radiation exposure to household members of patients receiving outpatient radioiodine therapy for hyperthyroidism or thyroid carcinoma were almost always well below the 5 mSv limit (5–8). No levels of contamination were found in home surveys by Panzegrau *et al*. (9), and patient satisfaction with outpatient therapy was high. Supporting the low potential for significant radiation exposure to the public are the data of Venencia *et al*. (10) who treated 14 patients with 30–221 mCi of ^{131}I and monitored them with dosimeters placed on the pectoral muscle. Using this dosimetry and assuming that another person was always 1 m from the treated patient (100% occupancy factor), their exposure did not approach 5.0 mSv until the treatment activity was greater than 187 mCi.

In this issue of *Thyroid*, Greenlee and colleagues (11) surveyed 311 endocrinologists, nuclear medicine physicians, surgeons, radiation safety officers, and other health professionals on behalf of the American Thyroid Association (ATA). The survey sought to identify the advice most commonly provided to patients receiving ^{131}I for hyperthyroidism, goiter, and thyroid cancer regarding the safety of others who could potentially be exposed to radiation from them. The majority of respondents were endocrinologists, from North America, and affiliated with universities. The survey offers a snapshot into current practice and highlights several areas of opportunity for education, harmonization, and communication between health-care providers and patients. The survey also has limitations. The respondents likely accounted for only a small fraction of those invited to respond or those involved in radioactive iodine treatment. Moreover, the similarities and differences between respondents and nonrespondents are not known. Respondents were not able to ask for questions to be clarified, and an explanation for why a respondent gave their answer was not provided. Additionally, although the study addressed therapeutic activity ranges for radioiodine, no distinction was made between treatments for hyperthyroidism, goiter, or thyroid cancer. These are situations in which the patient's uptake and retention of radioiodine over time are significantly different.

The survey results were reassuring in that within the first 24 hours after treatment, the majority of respondents indicated that they restricted exposure to young children, recommended that the patient limit time and proximity to others, avoid public transportation, and did not recommend staying in a hotel. They also recommended sleeping alone and avoiding sexual contact.

The survey also identified areas of concern and opportunities for improvement. For example, patients often receive radiation safety advice from multiple sources. Multiple sources of information are often a good thing, except when the recommendations disagree with each other. Only 50%–88% of respondents, however, could say that the information their patients receive from multiple sources was comparable. Similarly, there seemed to be a gap across the various disciplines regarding which care provider was ultimately responsible for providing the patient with radiation safety instructions.

Designing and interpreting survey questions can be a challenge. While most respondents indicated that they always screen for pregnancy before giving radioiodine, 9.5% indicated that they did this "sometimes." Perhaps these respondents do not screen for pregnancy in certain circumstances such as those who have been in menopause for many years or in very young children. It is surprising that some respondents accepted written or verbal patient statements of being not pregnant and quite concerning that one respondent indicated that they "never" screen for pregnancy. Also concerning was that 5%–11% of respondents apparently had no threshold to advise patients regarding certain practices to follow in the first 24 hours after treatment. These desirable practices include avoiding children ages 2–10 years of age, maintaining a specific time and/or distance from other people, and avoiding public transportation. Similarly, a small minority of respondents did not recommend to patients that they sleep alone or avoid sexual contact. Even more disconcerting is that 7% of respondents recommended avoiding breast-feeding only when the therapeutic activity was >30 mCi, while 27% reported that they did not advise patients to avoid breast-feeding, and half of the respondents apparently did not see a need to avoid breast-feeding beyond the first 48 hours after radioiodine treatment.

Most respondents stated they use a consent form for radioiodine administration, and most consent forms provided information on pregnancy, the need to avoid breastfeeding, and the risk to salivary glands. Still, nearly one third indicated that they did not use a consent form, and of those that did, 30%–40% did not include information about avoiding breast-feeding or the risk of salivary injury. Consent forms were more likely to be used by physicians in the United States (72%), but by only 58% of treating endocrinologists. In my opinion, patients receiving radioiodine (an irreversible event) are confronted with so much information during this stressful life experience that providing both verbal and written information seems both important and prudent. Further, a signed consent by both the patient (or guardian) and the treating health-care professional should document in layman's language the common or severe risks of treatment including the fact that this treatment should not be given if the patient is pregnant, lactating, or breast-feeding or expects to do so within a specified period of time. The consent form should also document that a discussion occurred regarding the benefits of treatment, alternative treatments, safety instructions, and follow-up plans. Finally, it should indicate that the patient's questions have been answered and that consent was given to receive ^{131}I treatment.

Since the NRC rule change to allow outpatient therapy with ^{131}I activities above 30 mCi, some have vocally questioned this practice and urged its repeal. Based on available data, the ATA believes the current NRC regulations regarding the therapeutic use of radioiodine are appropriate and safe. There is concern that repeal of the opportunity to use outpatient radioiodine therapy with activities greater than 30 mCi will increase medical costs and may impair or delay patient care. Also, there is additional concern that the need for hospitalization (rather than medical judgment) may influence the amount of radioiodine activity or eliminate its use entirely. At the same time, the ATA strongly supports individualized patient care and the liberty of patient hospitalization for treatment when medically indicated. These ATA opinions are consistent with those recently expressed by the NRC Advisory Committee on the Medical Use of Isotopes (12). The

ATA recognized the discordance of information given to patients as reflected in these survey results, or the lack of provided information suggested by other reports. To address this problem, the ATA has created a document that is under review for publication. The document "Radiation Safety in the Treatment of Patients with Thyroid Diseases by Radioiodine (^{131}I) Practice Recommendations of the American Thyroid Association" aims to provide simplified, consistent, and safe instructions for care providers and patients. The document includes an Eligibility Assessment Checklist, Precaution Requirement Examples, and Special Instructions for Radioiodine Safety for Patients. It is the intention of the ATA to help facilitate implementation and compliance with the current NRC regulations, provide education to professionals and patients, and promote the safety of the patient's family members and friends, the public, and healthcare providers based on the best scientific evidence available. To accomplish these goals, the ATA is grateful for the voluntary service and expertise of colleagues who designed, distributed, collected, analyzed, authored, and revised this survey manuscript, to those who completed the survey, and to those who have created our upcoming Practice Recommendations, which we hope will be recognized as a valuable resource.

Disclosure Statement

ATA opinions were approved by the ATA Board of Directors.

References

1. Tran P, Desimone S, Barrett M, Bachrach B 2010 I-131 treatment of Graves' disease in an unsuspected first trimester pregnancy; the potential for adverse effects on the fetus and a review of the current guidelines for pregnancy screening. Int J Pediatr Endocrinol **2010:**858359.
2. Nurnberger CE, Lipscomb A 1952 Transmission of radioiodine (I131) to infants through human maternal milk. JAMA **150:**1398–1400.
3. Kloos RT 2009 Protecting thyroid cancer patients from untoward effects of radioactive iodine treatment. Thyroid **19:**925–928.
4. Zablotska LB, Ron E, Rozhko AV, Hatch M, Polyanskaya ON, Brenner AV, Lubin J, Romanov GN, McConnell RJ, O'Kane P, Evseenko VV, Drozdovitch VV, Luckyanov N, Minenko VF, Bouville A, Masyakin VB. Thyroid cancer risk in Belarus among children and adolescents exposed to radioiodine after the Chornobyl accident. Br J Cancer 2010, E Pub.
5. de Carvalho JW, Sapienza M, Ono C, Watanabe T, Guimaraes MI, Gutterres R, Marechal MH, Buchpiguel C 2009 Could the treatment of differentiated thyroid carcinoma with 3.7 and 5.55 GBq of (131I)NaI, on an outpatient basis, be safe? Nucl Med Commun **30:**533–541.
6. Grigsby PW, Siegel BA, Baker S, Eichling JO 2000 Radiation exposure from outpatient radioactive iodine (^{131}I) therapy for thyroid carcinoma. JAMA **283:**2272–2274.
7. Marriott CJ, Webber CE, Gulenchyn KY 2007 Radiation exposure for 'caregivers' during high-dose outpatient radioiodine therapy. Radiat Prot Dosimetry **123:**62–67.
8. Pant GS, Sharma SK, Bal CS, Kumar R, Rath GK 2006 Radiation dose to family members of hyperthyroidism and thyroid cancer patients treated with 131I. Radiat Prot Dosimetry **118:**22–27.
9. Panzegrau B, Gordon L, Goudy GH 2005 Outpatient therapeutic 131I for thyroid cancer. J Nucl Med Technol **33:**28–30.
10. Venencia CD, Germanier AG, Bustos SR, Giovannini AA, Wyse EP 2002 Hospital discharge of patients with thyroid carcinoma treated with 131I. J Nucl Med **43:**61–65.
11. Greenlee MC, Burmeister LA, Butler R, Edinboro CH, Morrison S, Milas M 2011 Current safety practices relating to I-131 administration for diseases of the thyroid: a survey of physicians and allied practitioners. Thyroid **21:** 151–160.
12. Fisher D, Gilley D, Langhorst S, Mattmuller S, Suleiman O, Thomadsen B, Welsh J, Zanzonico P. Advisory Committee on the Medical Use of Isotopes (ACMUI) Patient Release Report. 12-13-2010. www.nrc.gov/about-nrc/regulatory/advisory/acmui.html (verified December 22, 2010).

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ATA Invites You to Join Us at the…

Registration Details

ATA meeting registration is open to all health care professionals interested in broadening their knowledge of the thyroid gland and its disorders. Meeting registration is opening in March 2011. **Visit the ATA website for agenda details and meeting information as available at *www.thyroid.org*.**

Why Should You Attend the 81st Annual Meeting of the ATA in Indian Wells, California?

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Where is the Meeting?

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Join the American Thyroid Association (ATA) for our newest educational initiative — a series of CME certified webinars beginning Tuesday, March 15, 2011 at 11:00 AM ET and recurring every **third Tuesday** of the month at 11:00 AM ET. CME Credit (*1 AMA PRA Category 1 Credit™) is* available for each webinar.

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David S. Cooper, MD
Johns Hopkins University
Tuesday, March 15, 2011, 11:00 AM ET

Practical Lessons from ATA Guidelines for the Management of Differentiated Thyroid Cancer
David S. Cooper, MD
Johns Hopkins University
Tuesday, April 19, 2011; 11:00 AM ET

Hypothyroidism LT4-LT3 Therapy
Michael T. McDermott, MD
University of Colorado Denver
Tuesday, May 17, 2011, 11:00 AM ET

Costs: $119 for ATA members per webinar/$149 for non-members per webinar. Discounts are available for registering for all three webinars as a package ($299 for ATA members and $379 for non-members). You can register to participate in the live streaming program or you can purchase a recording if you have a schedule conflict with the live broadcast.

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Call for Nominations for the 2011 Awards
American Thyroid Association

▪ Distinguished Service Award ▪ Sidney H. Ingbar Distinguished Lectureship ▪
▪ Van Meter Lecture ▪ Paul Starr Lecture •
• Lewis E. Braverman Lecture • John B. Stanbury Thyroid Pathophysiology Medal ▪

The Van Meter Award Lecture established in 1930, recognizes outstanding contributions to research on the thyroid gland or related subjects. The award is given each year to an investigator who is not older than the age of 45 in the year of the award. The Van Meter award winner is kept secret until the time of the award lecture during the annual meeting. An honorarium and expenses are awarded to the Van Meter recipient. This award receives support from Mary Ann Liebert, Inc., Publishers.

Nominee: Date of Birth

Sidney H. Ingbar Distinguished Lectureship Award, endowed by contributions to honor the memory of Sidney H. Ingbar, recognizes outstanding academic achievements in thyroidology, in keeping with the innovation and vision that epitomized Dr. Ingbar's brilliant investigative career. The Ingbar award is conferred upon an established investigator who has made major contributions to thyroid-related research over many years. An honorarium will be presented to the recipient.

Nominee:

The Paul Starr Award Lecture recognizes an outstanding contributor to clinical thyroidology. An honorarium will be presented to the recipient. This award receives support from Dr. Boris Catz.

Nominee:

The Distinguished Service Award (DSA) honors a member who has made important and continuing contributions to the American Thyroid Association (ATA). The DSA award certificate is presented at the ATA Annual Banquet.

Nominee:

The John B. Stanbury Thyroid Pathophysiology Medal recognizes outstanding research contributions, either conceptual or technical, to the understanding of thyroid physiology or the pathophysiology of thyroid disease, as evidenced by having a major impact on research or clinical practice related to thyroid diseases. A medal, funded by Dr. John Stanbury, is conferred at the Annual Banquet.

Nominee:

The Lewis E. Braverman Lectureship Award recognizes an individual who has demonstrated excellence and passion for mentoring fellows, students and junior faculty; has a long history of productive thyroid research; and is devoted to the ATA. The award is endowed by contributions to honor Dr. Lewis E. Braverman. An honorarium will be presented to the recipient.

Nominee:

Nominated by: (print or type) *Signature:* *Date:*

Nominators must submit all of the following electronically to thyroid@thyroid.org to complete the nomination by the deadline of March 31, 2011:

1. Completed and signed Nomination Form (above).
2. CV and brief nomination letter, emphasizing major accomplishments.
3. List of 2 to 4 most significant publications with PDF or URL to provide access to these papers.

Call for Nominations for 2011
American Thyroid Association
Board of Directors

In accordance with the Bylaws of the American Thyroid Association, the Nominating Committee is soliciting nominations from the membership for candidates for the offices of President and Directors (2) to serve on the ATA Board of Directors. Candidates will be selected by the Nominating Committee and submitted to the ATA Board in June 2011.

A ballot will be sent to the membership electronically in late August 2011. Newly elected Board members will be announced at the Annual Business Meeting on Thursday, October 27, 2011.

ATA President

The **President** will serve a one-year term as President-Elect (2011-2012), followed by one year as President (2012-2013), and another year as a Past-President (2013-2014). See job description in Policies and Procedures under "Members Only" at www.thyroid.org. *Election of the President will be competitive.*

Nominee: _____

ATA Board Director

Two **Directors** will each serve a four-year term (2011-2015). See job description in Policies and Procedures under "Members Only" at www.thyroid.org. *Election of directors will be competitive.*

Nominee: _____

Nominee: _____

Nominated by (please print or type): _____

Signature: Date:

All nominations must be submitted to the Executive Director, Bobbi Smith, by letter, fax, or e-mail bsmith@thyroid.org by April 30, 2011.

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