

# Thyroglobulin Guides Further Ablation After Cancer

*If a whole body scan is negative after surgery and ablation for thyroid cancer, Tg can guide iodine therapy.*

BY JEFF EVANS  
Senior Writer

CHANTILLY, VA. — Thyroid cancer patients who have received radioactive iodine ablation after thyroidectomy and who later have a negative whole body scan for thyroid cancer probably do not need to receive radioactive iodine therapy if their stimulated thyroglobulin levels stay below 10 ng/mL, Dr. R. Michael Tuttle said at the annual meeting of the Mid-Atlantic Chapter of the American Association of Clinical Endocrinologists.

Whether a patient with a very low stimulated thyroglobulin level should be treated again with radioactive iodine (RAI) “is probably one of the most common phone calls I get from around the country,” said Dr. Tuttle of Memorial Sloan-Kettering Cancer Center, New York.

The way thyroid cancer is treated today is “so remarkably different now than it was 10 or 15 years ago,” he said, adding that the detection of persistent thyroid cancer has improved to the point where thyroglobulin (Tg) levels of 1, 0.5, or 0.2 ng/mL can be detected and 3-mm lymph nodes in the tracheal-esophageal groove can be seen with ultrasound in patients who were thought to be cured 20 years ago.

“I can’t tell you the number of patients who leave my office mad at me because I’ve explained to them that I cannot cure their thyroid cancer. Their thyroglobulin level of 0.3 ng/mL is probably going to be there for awhile and taking out that 2-mm lymph node beside their recurrent laryngeal nerve is probably only going to help the surgeon and pathologist because they can bill and code for it, and it is unlikely to help our patient.”

About 80% of full body scans after repeat administration of therapeutic RAI appear to show some uptake by thyroid cells in the neck, but about 40% of these may

be lung metastases, based on experience with all forms of thyroid cancer. If physicians give 100-150 mCi of RAI to patients with a high Tg level but a negative body scan, “you’re very likely to find real disease,” Dr. Tuttle said, “and I think it’s that finding of the lung metastasis that made us all do this.”

## Rationale for RAI Changes Over Time

One rationale for using a therapeutic level of RAI when stimulated Tg levels remain high despite a negative diagnostic whole body scan was to localize the disease, not necessarily to treat it, Dr. Tuttle pointed out. Today’s imaging modalities of helical CT and PET scans and neck ultrasounds can give the same information that RAI scanning would, without the possibility of side effects.

There is no evidence that repeat RAI treatment for patients who have a high stimulated Tg level after an initially negative whole body scan increases disease-specific or overall survival, Dr. Tuttle said.

Most clinicians would give another course of therapeutic RAI if the stimulated Tg level rose above 10 ng/mL, and most would not use repeat RAI if the stimulated level was below 2 ng/mL. RAI treatment for Tg levels of less than 2 ng/mL offers little potential benefit, while potentially causing complications, including damage to salivary glands, taste buds, and tear ducts. “We don’t know what to do between 2 and 10,” Dr. Tuttle said.

Multiple RAI treatments appear to clear small-volume papillary thyroid cancer from pediatric to 30-year-old patients with positive lymph nodes by consistently decreasing stimulated Tg levels and clearing

evidence of the tumor on CT scans and x-rays. These patients, who do not have distant metastases, are either cured or go into long-term remissions.

But older patients with thyroid cancer extending beyond the thyroid are more commonly seen than are younger patients with less aggressive, localized disease. Older patients may have a negative whole body scan and the same level of Tg as a younger patient, but the tumor is likely to be visible in the lungs on x-ray, CT, and PET scans. RAI will not help these patients if the lung lesions are poorly differentiated.

In a soon-to-be published study, Dr. Tuttle found that of about 400 thyroid cancer

patients who received <sup>18</sup>fluorodeoxyglucose PET scans, the result of a PET scan was the most powerful prognostic indicator of survival. Patients with a markedly positive PET scan in extrathyroidal areas such as the lungs have a 3-year survival of less than 30%, he said.

**There is no evidence that repeat RAI after negative whole body scan increases survival.**

DR. TUTTLE

## Observe or Treat?

Another study involved 70 patients with thyroid cancer who had detectable Tg levels despite having a total thyroidectomy, RAI ablation, a negative whole body scan, and no structural evidence of disease. Of the 28 patients with a median stimulated Tg level of 9.5 ng/mL who were observed instead of being treated with RAI, 19 (68%) had an undetectable stimulated Tg level after 12 years of follow-up. Among the 42 patients with a median Tg level of 55 ng/mL who received RAI, only 12 (29%) had an undetectable stimulated Tg level after 7 years of follow-up (J. Clin. Endocrinol. Metab. 2001;86:4092-7).

Most patients who have undergone thyroidectomy and RAI ablation and have a negative whole body scan and a stimulated Tg level in the range of 2-10 ng/mL

will see their Tg level decline to an undetectable level, so they probably should not be treated subsequently with RAI, Dr. Tuttle advised. It is likely that “if you do nothing, you are going to take credit for this thyroglobulin number going down over time all by itself.”

It is not necessary to treat patients with high Tg levels with two to three doses of RAI, he added. In a study of 17 patients with a negative initial whole body scan and an elevated Tg level, 16 patients had a positive scan after RAI therapy. During the course of three subsequent RAI doses, the percentage of patients with a decreasing Tg level increased from 81% to 90% to 100%, but the mean stimulated Tg level only decreased from 74 to 62 to 32 ng/mL, respectively (J. Clin. Endocrinol. Metab. 1995;80:1488-92).

## Low Tg: RAI Probably Not Helpful

To determine if follow-up RAI therapy contributes to any changes in the stimulated Tg level of patients with an initial stimulated Tg level below 10 ng/mL, Dr. Tuttle conducted a study of 110 thyroid cancer patients who had Tg levels between 0.6 and 10 ng/mL and a negative whole body scan 1 year after receiving a total thyroidectomy and RAI ablation. At that point, 18 patients received repeat RAI therapy and 92 were observed.

After 1-2 years, stimulated Tg levels subsequently decreased in 71% and became undetectable in 29% of patients who had an initial stimulated Tg level between 0.6 and 2 ng/mL. In patients with an initial stimulated Tg level between 2 and 10 ng/mL, a significantly lower percentage of patients (3%) had an undetectable stimulated Tg level than those who had a decreased level (42%).

But among observed and RAI-treated patients with an initial stimulated Tg level between 2 and 10 ng/mL, there was no significant difference in the percentage of patients who had a reduction (40% vs. 45%, respectively), no change (12% vs. 18%), or an increase (48% vs. 37%) in their stimulated Tg level at follow-up. ■



# Subclinical Hypothyroidism Linked to Heart Failure in Elderly

BY MARY ANN MOON  
Contributing Writer

Elderly patients with subclinical hypothyroidism have a higher rate of congestive heart failure than do those who are euthyroid, according to Dr. Nicolas Rodondi of the University of California, San Francisco, and his associates.

Overt hypothyroidism is known to be associated with cardiovascular disease (CVD), but studies evaluating a possible link between subclinical hypothyroidism and CVD have produced conflicting results. Dr. Rodondi and his associates conducted what they described as the first prospective study to assess the risk of heart failure (HF) events in subjects with subclinical hypothyroidism.

The investigators assessed thyrotropin levels in 2,730 men and women aged 70-

79 years who were participating in a large cohort study of aging. The subjects were followed for 4 years to determine whether these hormone levels were related to HF or other cardiovascular disease events.

A total of 338 subjects (12.4%) were found to have subclinical hypothyroidism, defined as an elevated level of thyrotropin and a normal level of free thyroxine (T<sub>4</sub>). During follow-up, 178 subjects had HF events (Arch. Intern. Med. 2005;165:2460-6).

Subjects with moderately to severely elevated thyrotropin levels (7.0 mIU/L or greater) had more HF events (35 per 1,000 person-years) than did those who were eu-

thyroid (17 per 1,000 person-years). Each standard deviation increase of 4.0 mIU/L was associated with a 30% increase in HF events.

This link was stronger among subjects known to have previous HF events. The rate of recurrent HF events was seven times higher in those with subclinical hypothyroidism than in those who were euthyroid.

In contrast, subjects with mildly elevated thyrotropin (4.5-6.9 mIU/L) did not have higher HF event rates. Subclinical hypothyroidism was not found to be associated with other coronary heart disease events, stroke, peripheral arterial disease,

CVD-related mortality, or total mortality.

These results suggest that further study is warranted to determine whether subclinical hypothyroidism causes heart failure or worsens existing heart failure, Dr. Rodondi and his associates said.

In an editorial that accompanied the article, Dr. Lawrence M. Crapo of Santa Clara Valley Medical Center, San Jose, Calif., noted these findings “certainly support the idea that the treatment of severe subclinical hypothyroidism with levothyroxine in patients younger than 80 years may be beneficial, but this remains to be proved in a randomized prospective therapeutic trial.”

The results further indicate that patients with mild hypothyroidism probably would not benefit from levothyroxine treatment, Dr. Crapo said (Arch. Intern. Med. 2005;165:2451-2). ■

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