

Update on thyroid cancer surveillance and management of recurrent disease

Minimally invasive thyroid surgery

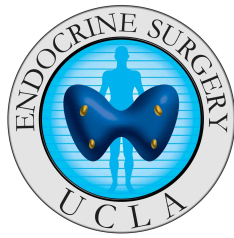
July 2006

Michael W. Yeh, MD

Program Director, Endocrine Surgery

Assistant Professor, David Geffen School of Medicine at UCLA

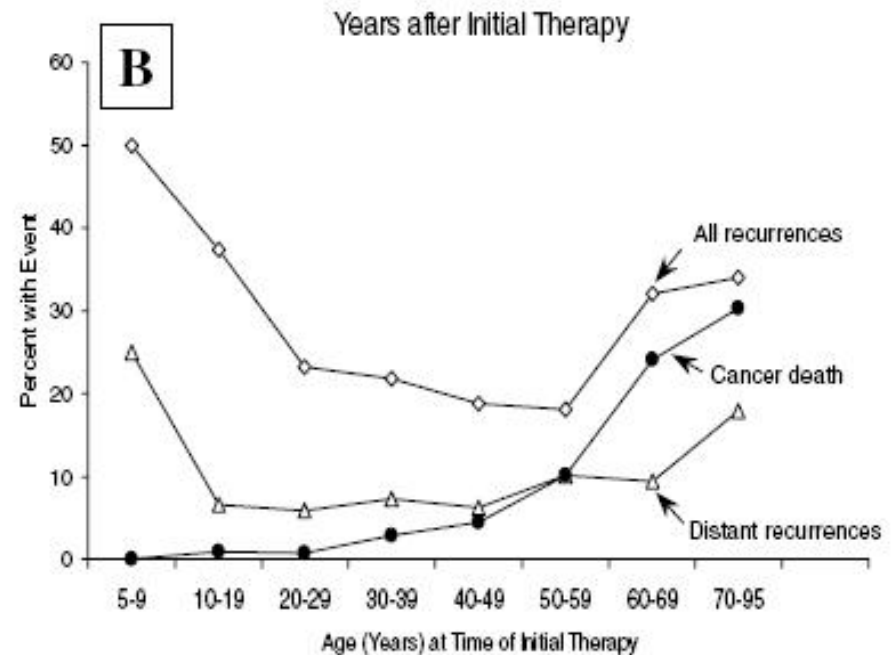
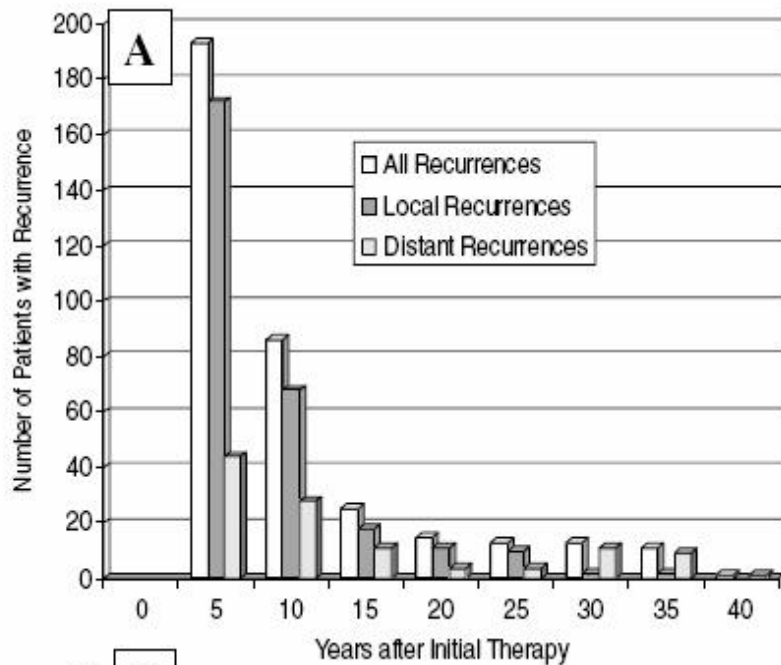
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Differentiated thyroid cancer

- Prognosis highly favorable
 - Overall survival: papillary 98%, follicular 92%
- Median age at diagnosis 45
- 25% lifetime recurrence risk
- Increased mortality assoc. with recurrence
- PTC metastasizes to regional lymph nodes
- FTC to lymph nodes and distant sites

Thyroid cancer recurrence



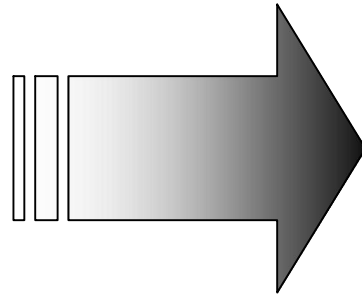
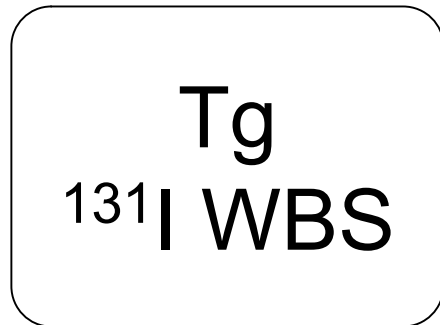
Mazzaferri EL & Kloos RT 2002 Is diagnostic iodine-131 scanning with recombinant human TSH (rhTSH) useful in the follow-up of differentiated thyroid cancer after thyroid ablation? *Journal of Clinical Endocrinology and Metabolism* **87** 1490–1498.

Monitoring for recurrence

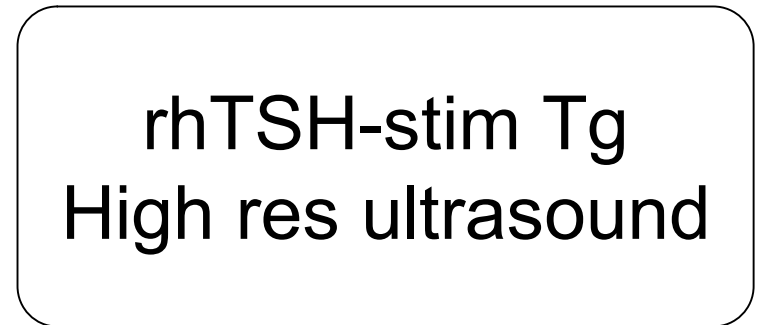
- Biochemical tests
 - Thyroglobulin (Tg)
 - Stimulated (thyroxine withdrawal vs. rh-TSH)
 - Problem of interfering antibodies
- Anatomic imaging (US, MRI, CT)
- Functional imaging (^{131}I WBS, PET)

Paradigm shift in monitoring strategy

Pre-2000



Post-2000



Rationale for the shift: Part 1

- Several large studies demonstrate that ^{131}I WBS has low sensitivity for detection of locoregional metastases (19%)
- ^{131}I WBS results to not alter management in the subsequent care of patients with DTC
- WBS only detects any thyroid remnant after surgery. Metastases more effectively detected by US and Tg.

1. Cailleux, A.F., et al., *Is diagnostic iodine-131 scanning useful after total thyroid ablation for differentiated thyroid cancer?* J Clin Endocrinol Metab, 2000. **85**(1): p. 175-8.
2. Pacini, F., et al., *Diagnostic 131-iodine whole-body scan may be avoided in thyroid cancer patients who have undetectable stimulated serum Tg levels after initial treatment.* J Clin Endocrinol Metab, 2002. **87**(4): p. 1499-501.
3. Pacini, F., et al., *Recombinant human thyrotropin-stimulated serum thyroglobulin combined with neck ultrasonography has the highest sensitivity in monitoring differentiated thyroid carcinoma.* J Clin Endocrinol Metab, 2003. **88**(8): p. 3668-73.
4. Torlontano, M., et al., *Follow-up of low risk patients with papillary thyroid cancer: role of neck ultrasonography in detecting lymph node metastases.* J Clin Endocrinol Metab, 2004. **89**(7): p. 3402-7.
5. Torlontano, M., et al., *Comparative evaluation of recombinant human thyrotropin-stimulated thyroglobulin levels, 131I whole-body scintigraphy, and neck ultrasonography in the follow-up of patients with papillary thyroid microcarcinoma who have not undergone radioiodine therapy.* J Clin Endocrinol Metab, 2006. **91**(1): p. 60-3.
6. Torlontano, M., et al., *Serum thyroglobulin and 131I whole body scan after recombinant human TSH stimulation in the follow-up of low-risk patients with differentiated thyroid cancer.* Eur J Endocrinol, 2003. **148**(1): p. 19-24.
7. Mazzaferri, E.L., et al., *A consensus report of the role of serum thyroglobulin as a monitoring method for low-risk patients with papillary thyroid carcinoma.* J Clin Endocrinol Metab, 2003. **88**(4): p. 1433-41.

Rationale for the shift: Part 2

- Ultrasound increasingly sensitive
- Acceptance of rh-TSH stimulated Tg testing

Recombinant Human Thyrotropin-Stimulated Serum Thyroglobulin Combined with Neck Ultrasonography Has the Highest Sensitivity in Monitoring Differentiated Thyroid Carcinoma

F. PACINI, E. MOLINARO, M. G. CASTAGNA, L. AGATE, R. ELISEI, C. CECCARELLI, F. LIPPI, D. TADDEI, L. GRASSO, AND A. PINCHERA

Section of Endocrinology, Department of Endocrinology and Metabolism, University of Pisa (E.M., M.G.C., L.A., R.E., C.C., F.L., D.T., L.G., A.P.), 56124 Pisa, Italy; and Section of Endocrinology and Metabolism, Department of Internal Medicine, Endocrinology and Metabolism, and Biochemistry, University of Siena (F.P.), 53100 Siena, Italy

Recombinant human TSH (rhTSH)-stimulated thyroglobulin (Tg) measurement and ^{131}I whole body scan (WBS) have been validated as informative tests in the postsurgical follow-up of differentiated thyroid carcinoma. We report the diagnostic accuracy of Tg measurement and diagnostic WBS, alone or in combination, after rhTSH stimulation in a retrospective, consecutive series of patients undergoing follow-up for differentiated thyroid cancer. Routine procedures also include neck ultrasound in every patient and post-therapy WBS when indicated. We studied 340 consecutive patients with differentiated thyroid carcinoma, previously treated with near-total thyroidectomy and ^{131}I thyroid ablation, scheduled for routine diagnostic tests. At baseline on L-T₄-suppressive therapy, 294 patients had undetectable (<1 ng/ml) serum Tg and negative anti-Tg autoantibodies (TgAb), 25 patients had undetectable serum Tg and positive TgAb, and 21 patients had detectable serum Tg and negative TgAb. These patients were

tested for the presence of active disease by rhTSH stimulation. The results of our study showed that rhTSH-stimulated Tg alone had a diagnostic sensitivity of 85% for detecting active disease and a negative predictive value (NPV) of 98.2%. After adding the results of neck ultrasound, sensitivity increased to 96.3%, and the NPV to 99.5%. rhTSH-stimulated WBS had a sensitivity of only 21% and a NPV of 89%. The combination of rhTSH-stimulated Tg and WBS had a sensitivity of 92.7% and a NPV of 99%. We conclude that the rhTSH-stimulated Tg test combined with neck ultrasonography has the highest diagnostic accuracy in detecting persistent disease in the follow-up of differentiated thyroid carcinoma. A detectable level of serum Tg on L-T₄, its conversion from undetectable to detectable after rhTSH, and/or a suspicious finding at ultrasound will allow the identification of patients requiring therapeutic procedures without the need for diagnostic WBS. (*J Clin Endocrinol Metab* 88: 3668–3673, 2003)

What are the roles of diagnostic whole-body radioiodine scans, ultrasound, and other imaging techniques during follow-up of differentiated thyroid cancer?

After radioiodine ablation, subsequent DxWBS have low sensitivity and are usually not necessary in low-risk patients who are clinically free of residual tumor and have an undetectable serum thyroglobulin level during thyroid hormone suppression of serum TSH and negative cervical ultrasound.

After surgery, cervical ultrasound to evaluate the thyroid bed and central and lateral cervical nodal compartments should be performed at 6 and 12 months and then annually for at least 3–5 years, depending on the patients' risk for recurrent disease and thyroglobulin status.

2006 ATA management guidelines for DTC

What is the role of serum thyroglobulin assays in the follow-up of differentiated thyroid cancer?

Serum thyroglobulin has a high degree of sensitivity and specificity to detect thyroid cancer, especially after total thyroidectomy and remnant ablation, with the highest degrees of sensitivity noted after thyroid hormone withdrawal or stimulation using recombinant human thyrotropin (rhTSH).

2006 ATA management guidelines for DTC

A Single Recombinant Human Thyrotropin-Stimulated Serum Thyroglobulin Measurement Predicts Differentiated Thyroid Carcinoma Metastases Three to Five Years Later

The positive predictive value of the initial rhTSH-Tg greater than 2 ng/ml was 80%, and the negative predictive value was 98%.

Kloos, R.T. and E.L. Mazzaferri, J Clin Endocrinol Metab, 2005. **90**(9): p. 5047-57.

What is the most appropriate management of patients with metastatic disease?

Patients with persistent/recurrent disease confined to the neck should undergo complete ipsilateral or central compartmental dissection of involved compartments while sparing vital structures.

Approximately one third to one half of patients may become free of disease in short-term follow-up.

Patients who underwent treatment and became free of disease were 3-fold as likely to have become so after additional surgery compared with additional ¹³¹I treatment.

Treatment and follow up of DTC in 2006

- Early detection, complete resection, ^{131}I ablation
- Stim-Tg testing within 1 yr
- Tg < 2: Great!
- Tg > 2: Ultrasound
- FNA of detectable lesions
- Surgery to clear metastases, \pm further ^{131}I
- Periodic stim-Tg testing and US

Minimally invasive thyroid surgery

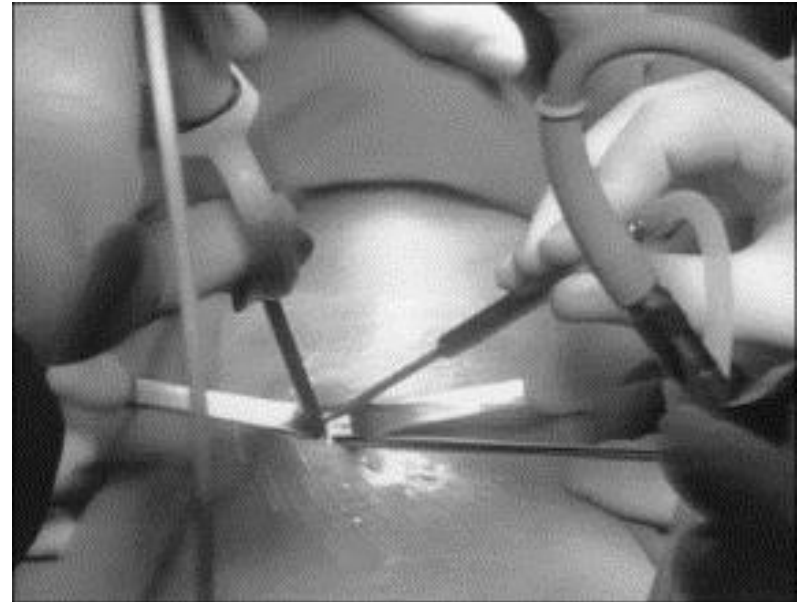
“We propose that this term be used only to describe thyroid and parathyroid procedures that are routinely associated with an incision shorter than 3.0 cm for thyroidectomy and 2.5 cm for parathyroidectomy.”

Brunaud L, Zarnegar R, Wada N, Ituarte P, Clark OH, Duh QY. Incision length for standard thyroidectomy and parathyroidectomy: when is it minimally invasive? Arch Surg. 2003 Oct;138(10):1140-3.

Comparison between minimally invasive video-assisted thyroidectomy and conventional thyroidectomy: A prospective randomized study

Paolo Miccoli, MD, Piero Berti, MD, Marco Raffaelli, MD, Gabriele Materazzi, MD, Silvia Baldacci, BS, and Giuseppe Rossi, PhD, *Pisa, Italy*

- Reduced pain
- Improved cosmetic results
- Longer operation
- Stringent patient selection
- Similar complication rates
- Not standard of care for cancer



Minimally invasive thyroid surgery

F. Fausto Palazzo
Mark S. Sywak
Stan B. Sidhu
Leigh W. Delbridge

Langenbecks Arch Surg
(2005) 390: 230–235

Safety and feasibility of thyroid lobectomy via a lateral 2.5-cm incision with a cohort comparison of the first 50 cases: evolution of a surgical approach

