



FIVE-YEAR SURVIVAL IS SIMILAR IN THYROID CANCER PATIENTS WITH DISTANT METASTASES PREPARED FOR RADIOACTIVE IODINE THERAPY WITH EITHER THYROID HORMONE WITHDRAWAL OR RECOMBINANT HUMAN THYROTROPIN.....2

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Clinical Thyroidology

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Clinical THYROIDOLOGY

VOLUME 23 • ISSUE 8

AUGUST 2011

FIVE-YEAR SURVIVAL IS SIMILAR IN THYROID CANCER PATIENTS WITH DISTANT METASTASES PREPARED FOR RADIOACTIVE IODINE THERAPY WITH EITHER THYROID HORMONE WITHDRAWAL OR RECOMBINANT HUMAN THYROTROPIN

Tala H, Robbins R, Fagin JA, Larson SM, Tuttle RM. **Five-year survival is similar in thyroid cancer patients with distant metastases prepared for radioactive iodine therapy with either thyroid hormone withdrawal or recombinant human TSH.** J Clin Endocrinol Metab. May 11, 2011 [Epub ahead of print].

SUMMARY

BACKGROUND

Randomized trials have demonstrated that radioactive iodine (RAI) ablation of thyroid remnants is equally facilitated by withdrawal from thyroid hormone, inducing hypothyroidism, and by administration of recombinant human thyrotropin (rhTSH) (1,2). Reports have suggested that small-volume local nodal disease identified incidentally after remnant ablation appears to be effectively treated by either withdrawal or rhTSH preparation (2,3). This is a retrospective study to determine whether there is a difference in the short-term survival of patients with iodine-avid thyroid cancer metastatic to bone or lung (American Joint Committee on Cancer stage IV) and treated with RAI after either TH-WD or rhTSH administration.

METHODS

This 17-year retrospective study, conducted from 1993 through 2010, involved 175 patients with differentiated thyroid cancer with iodine-avid metastatic disease to bone (28%), lung (52%) or both (19%). Patients were excluded if the tumor was anaplastic or not iodine-avid or if there was metastatic disease to other organs. Patients were also excluded if there was inadequate follow-up or other malignancies or if the patients was <20 years old.

All patients treated with RAI for distant metastases were placed on a low-iodine diet and underwent formal whole-body and blood RAI clearance dosimetry studies to calculate a dose that delivered <2 Gy to the bone marrow and had less than 80 mCi whole-body retention at 48 hours. Thirty-eight patients had received one or more doses of RAI after thyroid hormone withdrawal prior to referral to the authors' center. Patients treated before 1998 received RAI after withdrawal; starting in 1998, when rhTSH became commercially available,

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disease possibly will not result in the same results as achieved at this premier institution for thyroid cancer care. I cannot conclude that patients with iodine-avid distant disease will be adequately treated with rhTSH and empirical doses of RAI, but it is fair to say that a four-dose rhTSH-stimulated dosimetry-

determined treatment with RAI for a patient with RAI-avid metastatic disease appears to be a reasonable alternative to traditional thyroid hormone withdrawal RAI treatments.

— **Stephanie L. Lee, MD, PhD**

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HYPERTHYROIDISM DUE TO HCG OCCURS IN 2% OF CASES OF GESTATIONAL TROPHOBLASTIC DISEASE

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A PET/CT THAT IS NEGATIVE MAY BE A COST-EFFECTIVE MODALITY TO AVOID UNNECESSARY SURGERY FOR NODULES WITH NONDIAGNOSTIC CYTOLOGY

Giovanella L, Suriano S, Maffioli M, Ceriani L. **¹⁸F-DG-positron emission tomography/computed tomography (PET/CT) scanning in thyroid nodules with nondiagnostic cytology.**
Clin Endocrinol 2011;74:644-8.

SUMMARY ●●●●●●●●●●●●●●●●

BACKGROUND

Many patients with thyroid nodule fine-needle aspiration (FNA) cytology that is classified as nondiagnostic are put through surgery despite having a benign nodule. This article examines the role of ¹⁸F-fluorodeoxyglucose-positron-emission tomography/computed tomography (¹⁸F-FDG-PET/CT) as a tool to determine whether the nodule can be classified as benign despite the nondiagnostic cytology. It should be noted that the nondiagnostic category is not the indeterminate category. Nondiagnostic usually implies insufficient material for diagnosis and is reported in 5% to 20% of FNA biopsies.

METHODS

In this study, 1648 patients with normal thyrotropin (TSH) levels and a single thyroid nodule >10 mm with suspicious ultrasound characteristics (hypoechoic nodule, >10 mm, irregular margins, chaotic intranodular vascular spots, a shape that was round or more tall than wide, microcalcifications) underwent ultrasound-guided FNA between January 2006 and June 2010. Patients had ¹⁸F-FDG-PET/CT after a 6-hour fast. Any visually discernible ¹⁸F-FDG uptake within the thyroid nodule (above thyroid tissue background) was classified as positive.

RESULTS

A total of 151 of the 1648 patients (9.2%) had nondiagnostic results and FNA was repeated. Of

these 151 patients, 88 (58%) had results that were still nondiagnostic and were enrolled in the study (61 women, 27 men; mean [±SD] age, 43.5±11.7 years; range, 18 to 79). All 88 patients had ¹⁸F-FDG-PET/CT before they were sent for surgery, and all 88 underwent lobectomy. Histologic analysis of the surgical specimen showed 29 patients (33%) with malignant lesions and 59 (67%) with benign lesions.

Twenty-nine patients with thyroid malignancies had a positive ¹⁸F-FDG-PET/CT scan with focal ¹⁸F-FDG uptake within the nodule. Among 59 patients with histologically proven benign nodules, 35 displayed no uptake, 16 displayed focal uptake, and 8 (all affected by autoimmune thyroiditis) displayed diffuse or diffuse plus focal uptake.

The sensitivity of ¹⁸F-FDG-PET/CT was 100%, the specificity 69%, the accuracy 79%, the positive predictive value 62%, and the negative predictive value 100%.

CONCLUSIONS

A negative ¹⁸F-FDG-PET/CT scan rules out malignancies among thyroid nodules with nondiagnostic cytology and can serve as a basis to avoid surgical excision. Surgery is still necessary to distinguish benign from malignant disease in nodules that are FDG-positive. Unnecessary surgery could have been reduced from 88 to 41 patients (46%) in this study.

COMMENTARY ●●●●●●●●●●●●●●●●

¹⁸F-FDG-PET/CT is mainly used in the evaluation of patients with metastatic cancer. The role of ¹⁸F-FDG-PET/CT in the treatment of thyroid cancer is limited, and it is used primarily in the postoperative

surveillance of patients with differentiated thyroid cancer with positive thyroglobulin and negative radioiodine scans (1). Other indications are initial staging and follow-up of high-risk patients with poorly differentiated thyroid cancer with negative

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A PET/CT THAT IS NEGATIVE MAY BE A COST-EFFECTIVE MODALITY TO AVOID UNNECESSARY SURGERY FOR NODULES WITH NONDIAGNOSTIC CYTOLOGY

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radioiodine scans (2). ¹⁸F-FDG-PET/CT also is useful, though somewhat limited, in the evaluation of thyroid nodules with suspicious features on ultrasound.

The ATA guidelines state that patients with nondiagnostic FNA should get a second FNA that is ultrasound-guided (2). The second FNA should be performed 3 months after the initial test (3). If the nodule is partially cystic with some suspicious characteristics, one may elect to follow the patient closely or recommend surgical excision, whereas a solid nodule should be more strongly considered for surgical evaluation after two nondiagnostic FNAs (2, 3). FNA is nondiagnostic in 5% to 20% of cases (4) and repeat FNA under ultrasound guidance may provide a diagnostic specimen in 75% of solid nodules and 50% of cystic nodules (5). A third ultrasound-guided FNA is less likely to be diagnostic.

Because only 6% to 20% of patients who have thyroid nodules with nondiagnostic FNA results have thyroid cancer (6, 7), the vast majority of the patients are subjected to unnecessary surgery to rule out malignancy. Negative results on ¹⁸F-FDG-PET/CT may be a cost-effective way to avoid unnecessary surgery.

— **Muhammad Salman ul Haq, MD**
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— **Jerome M. Hershman, MD**

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AFTER IODINE-131 THERAPY FOR DIFFERENTIATED THYROID CANCER, INFERTILITY IS LOW AND OBSTETRICAL AND NEONATAL OUTCOMES ARE VERY GOOD

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ADDISON'S DISEASE IS MORE CLOSELY ASSOCIATED WITH HASHIMOTO'S THAN WITH GRAVES' DISEASE

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INCREASED DIETARY INTAKE OF NITRATE MAY CAUSE THYROID CANCER IN MEN

Kilfoy BA, Zhang Y, Park Y, Holford TR, Schatzkin A, Hollenbeck A, Ward MH. **Dietary nitrate and nitrite and the risk of thyroid cancer in the NIH-AARP Diet and Health Study.** *Int J Cancer* 2011;129:160-72. doi: 10.1002/ijc.25650. Epub November 18, 2010.

SUMMARY ●●●●●●●●●●●●●●●●●●●●

BACKGROUND

The incidence of thyroid cancer has been increasing during the past few decades. Ionizing radiation is the only well-established causative factor. The present study considered the possibility that nitrate and nitrite intake could play a role, based on the fact that nitrate competitively inhibits iodide transport into the thyroid gland. Also, nitrate is reduced to nitrite by oral bacteria, and nitrite reacts with amines and amides in vivo to form nitrosamines and nitrosamides that are potent carcinogens for animals.

METHODS

The authors used a database of the NIH-AARP Diet and Health Study that was initiated in 1995–1996 when an extensive baseline questionnaire was mailed to 3.5 million AARP members 50 to 71 years of age. A total of 567,169 questionnaires were determined to have been satisfactorily completed. The nitrate and nitrite content of over 3000 foods was determined by review of the literature. Based on a food-frequency questionnaire, the nitrate and nitrite intake of each person was calculated. The major contributors to nitrate intake were lettuce, spinach, and broccoli, and the major contributors to nitrite intake were cold cuts, pasta, and bread. A total of 370 cases of thyroid cancer were identified in this population during a

7-year span, 200 in women and 170 in men; 70% were papillary cancers.

RESULTS

The incidence of thyroid cancer was 17 in 100,000 patient-years. The mean dietary nitrate intake was 88 mg/day and the mean nitrite intake was 1.2 mg/day. Among men in the highest quintile of nitrate intake, there was a 2.3-fold increased risk of thyroid cancer (95% confidence interval [CI], 1.3 to 4.0). There was a 3-fold increased risk of follicular thyroid cancer in men in the highest quartile of nitrate intake, but this was not found in women. Nitrite intake was associated with an increased trend for follicular thyroid cancer in men but not in women. A borderline significant interaction was found for smoking status and nitrite intake in women with a nonsignificant trend for thyroid cancer in the highest quintile of nitrate and nitrite intake.

CONCLUSIONS

Among men, increasing nitrate intake was positively associated with thyroid cancer, with a relative risk of 2.3 for the highest quintile versus the lowest (95% CI, 1.3 to 4.0), but there was no significant trend with intake among women. Nitrite intake was not associated with risk of thyroid cancer for either men or women.

COMMENTARY ●●●●●●●●●●●●●●●●●●●●

Studies to explain the increasing incidence of thyroid cancer are worthwhile. The hypothesis tested by this study is based on the finding that nitrate competitively inhibits iodide uptake by the thyroid. Furthermore, reduced iodide uptake causes increased thyrotropin stimulation, and this could promote thyroid carcinogenesis. Studies with cultured cells that con-

tained the sodium-iodide symporter showed that nitrate has about one eighth the affinity of iodide for the symporter (1). Although thiocyanate generated from smoking was thought to be the main anionic inhibitor of iodide uptake (1), nitrate could also play a significant role. Because the main source of dietary nitrate is leafy vegetables, it is possible that pesticides used in agriculture may be responsible for promoting thyroid cancer.

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The finding that higher nitrate intake increases the risk for thyroid cancer in men but not in women requires explanation. The same group found a significant association of nitrate intake with thyroid cancer in older women in Iowa (2) and could not offer an explanation for not corroborating this finding in


the present larger study. I agree with the conclusion that the role of nitrate in thyroid carcinogenesis is worthy of further study.

— Jerome M. Hershman, MD


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WHY DID TSH RECEPTOR MUTATIONS THAT CAUSED FRANK HYPOTHYROIDISM IN A PATIENT CAUSE ONLY SUBCLINICAL TSH RESISTANCE IN HER SIBLING?

Narumi S, et al.

COMMENTARY ●●●●●●●●●●●●●●●●

Defective Gq coupling should impair the generation of H₂O₂, and the increased level of TSH would be expected to increase sodium/iodide symporter activity, among other things. Some impairment in organification might have been expected, although the perchlorate discharge test was negative in the girl. However, her brother—who has the same compound heterogeneous mutations—had a normal ¹²³I uptake. The difference in sex between siblings could be an issue, although no sex difference in the ¹²³I uptake has been noted in R450H homozygotes (1,2). Indeed the thyroid defect in homozygotes does not appear very different from what is reported in heterozygotes, other than perhaps a slightly higher dose of L-T₄ being required in some cases (1). In addition, a recent Korean study used technetium-99m-pertechnetate (^{99m}TcO₄) uptake measurements before treatment to categorize 193 neonates with permanent congenital hypothyroidism. Of 79 whose ^{99m}TcO₄ uptake was less than 2.5%, 13 were found to have TSHR mutations,

7 being the R450H mutation. In contrast, of 114 whose uptake was greater than 2.5%, only one had R450H, and of the 68 whose uptake was greater than 7%, none had R450H (2). However, there is a recent wrinkle to the Gq story: it now seems that before the TSH receptor can couple with Gq, the TSHR must be dimerized, and then two molecules of TSH must bind to the dimer (3). This raises the issue of how well a mutant TSHR allele can dimerize with the normal TSHR and also with itself.

Whatever the underlying cause, a recent Greek study reported that over 70% of 3- to 5-day-old infants whose TSH is between 10 and 20 mU/L will turn out to have permanent hypothyroidism when reassessed at 3 years (4). This supports the belief that newborns with mild TSH elevations who have a mutation in their TSH receptor probably should be given L-T₄ replacement, even if their thyroid hormone levels are normal (1).

— Stephen W. Spaulding

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

HOTEL

Book your hotel reservation now and mention the ATA to receive the special group rate. Renaissance Esmeralda Resort & Spa, 44-400 Indian Wells Lane, Indian Wells, CA 92210; 760-773-4444 or 800-446-9875.

Call for Abstracts



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Call for Abstracts Submission Deadlines

- Regular call: Site opens – Wednesday, April 27, 2011
Site closes – Wednesday, June 22, 2011
Acceptance notification – Monday, July 25, 2011
- Short call: Site opens – Wednesday, September 7, 2011
Site closes – Wednesday, September 21, 2011
Acceptance notification – Monday, September 26, 2011

ATA Abstract Submission Policy and Responsibilities of the Author: The ATA requests submission of abstracts for consideration at ATA scientific meetings to feature new data presented as posters or oral presentations. The ATA goal is to provide the audience and the media with new data that are unpublished (in print or electronic) which are being publicly presented for the first time. Authors are asked to strictly comply with this requirement; data that are to become available to the public *in the setting of a national or international meeting* before their presentation at the ATA meeting are not eligible for presentation at the ATA meeting. Data may be submitted for publication before or after abstract submission to the ATA. However, data accepted for publication prior to the ATA meeting would REQUIRE the authors to request the publisher to embargo their publication (electronic and print) until **8:00 am local time the first day of the meeting**, or would REQUIRE the authors to withdraw their abstract from the ATA meeting. Many editors are favorable to embargo requests because of the attention that may be drawn to the publication after original presentation of the data at a major meeting. Further, the authors are welcome to announce the date and place of their anticipated publication if known. Authors that do not comply with this policy may be restricted from future abstract submissions for a term to be determined by the ATA Executive Committee. Arbitration, if needed, will occur via the ATA Board of Directors. **Abstracts are reviewed in confidence by the ATA program committee with possible ad hoc members.**

Additional policies:

- **CHARACTER LIMIT:** There is a limit of 2,245 characters (approx. 300 words) for the text of your submission.
- Authors of accepted posters are required to be present during the assigned poster sessions.
- Scientific materials presented at the ATA Annual Meeting must not have been submitted for publication at the time of abstract submission or presented at a scientific meeting before the 81st Annual Meeting of the ATA (local and regional meetings excluded).
- All abstracts must be filed electronically via the American Thyroid Association website www.thyroid.org. Submissions will not be accepted by fax or mail.
- All materials must arrive on or before the abstract deadlines noted above.
- Authorship on multiple abstracts is permitted.

Short Call Abstracts

- Short Call Abstracts are reserved for the presentation of the very latest, important thyroid-related research with high impact. Submission of a Short Call Abstract does not guarantee acceptance for presentation. (Please note that regular research reports should be submitted by the Regular Abstract deadline.)
- Only Six (6) Short Call Abstracts will be selected for 10-minute oral presentations during a special symposium. Selected additional Short Call Abstracts may be presented as special posters. All other submissions will not be published.
- Acceptance notices for those selected will be e-mailed on or before September 26, 2011. Online confirmation is required.

American Thyroid Association

Dedicated to Scientific Inquiry, Clinical Excellence, Public Service, Education, and Collaboration

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LIVE COURSES FREE TO FELLOWS

New Technologies and Techniques in Thyroid Surgery

Tuesday, September 20, 2011; 11:00 AM ET

William B. Inabnet, III, MD, FACS

Mount Sinai Medical Center

1 CME Credit Available

The field of thyroid surgery has experienced numerous advances since the advent of laparoscopic surgery in the early 1990's. This webinar will provide a comprehensive update on new techniques and technology in thyroid surgery with an emphasis on minimally invasive and video-endoscopic approaches to the thyroid gland. A pathway for safely introducing new techniques to the clinical realm will be discussed. [Learn More...](#)

Costs: \$119 for ATA members per webinar/\$149 for non-members per webinar. **Free registration for all fellows who sign up for the 9/20/2011, 11:00 AM ET live webinar.**

Fellows should contact the ATA at thyroid@thyroid.org to receive the complimentary registration code to participate.



Target Audience (Who Should Attend): ATA webinars are designed for endocrinologists, internists, surgeons, basic scientists, nuclear medicine scientists, pathologists, endocrine and surgery fellows, nurses, physician assistants and other health care professionals who wish to broaden and update their knowledge of the thyroid gland and its disorders including clinical management guidelines and recent advances in thyroidology.

Learning Objectives: At the conclusion of ATA webinars, attendees should be able to:

- Describe state-of-the art findings on the mechanisms, prevention, diagnosis, and management of thyroid disorders and cancer
- Explain the latest clinical management guidelines to benefit patient care and the expertise of the clinician in practice
- Describe the impact of health policy, environmental factors, genetic factors, and non-thyroidal conditions on thyroid disorders and cancer
- Explain new treatment options for thyroid disorders and cancer in patient care
- Identify opportunities for increasing education and collaboration to further understand thyroid disorders, thyroid cancer and managing patient care

Disclosures: Disclosures for presenting faculty and content controllers will be provided to attendees verbally or on-screen during the live webinar activity.

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The banner features a scenic background image of a resort with mountains and a lake. On the right side, there is a circular logo containing a stylized butterfly or 'W' shape, representing the American Thyroid Association. Below the logo, the text 'AMERICAN THYROID ASSOCIATION' and 'FOUNDED 1923' is displayed.