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Clinical Thyroidology

EDITORS' COMMENTS

This is the twelfth 2010 issue of *Clinical Thyroidology*.

We are happy to announce that Dr. Jerome M. Hershman will assume the role of Editor-in-Chief of *Clinical Thyroidology* in January 2011.

EDITORS' CHOICE ARTICLES are particularly important studies that we recommend you read in their entirety.

SEARCH FOR PREVIOUS ISSUES OF *Clinical Thyroidology* Many of our readers have asked for a quick way to find articles published in this journal over the past years. Now you can access previous issues using key words, author names, and categories such as Hyperthyroidism, Thyroid cancer, or other terms pertaining to thyroidology. You will find this by simply clicking the following URL: http://thyroid.org/professionals/publications/clinthy/index.html.

FIGURES The articles in *Clinical Thyroidology* contain figures with the ATA logo and a CT citation with the volume and issue numbers. We encourage you to continue using these figures in your lectures, which we hope will be useful to you and your students.

WHATS NEW On the last page of the journal, in addition to the section HOT ARTICLES AND REVIEWS, we have added CURRENT GUIDELINES that have relevance to thyroidologists, endocrinologists, surgeons, oncologists, students, and others who read this journal. We hope you will find this useful.

We thank our readers for their feedback and suggestions over the past years, and to the contributors to *Clinical Thyroidology*.

Sincerely,
Ernest L. Mazzaferri, MD, MACP

How to navigate this document: The Table of Contents and the Bookmarks are linked to the articles. To navigate, move your cursor over the article title you wish to see (either in the Contents or in the Bookmarks panel) and the hand will show a pointing finger, indicating a link. Left-click the title and the article will instantly appear on your screen. To return to the Contents, move the cursor to the bottom of the page and left-click Back to Contents which appears on every page. If you would like more information about using Bookmarks please see the help feature on the menu bar of Acrobat Reader.

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Preparation with recombinant human TSH or thyroid hormone withdrawal has similar therapeutic (tumoricidal) effects on small-volume metastases discovered incidentally during remnant ablation

Tuttle RM, Lopez N, Leboeuf R, Minkowitz SM, Grewal R, Brokhin M, Omry G, Larson S. Radioactive iodine administered for thyroid remnant ablation following recombinant human thyroid stimulating hormone preparation also has an important adjuvant therapy function. Thyroid 2010;20:257-63.

SUMMARY

BACKGROUND

Recombinant human thyrotropin (rhTSH) has been approved by the Food and Drug Administration (FDA) since 2007 for preparing patients for radioiodine (^{131}I) remnant ablation (RRA) after total thyroidectomy in well-differentiated thyroid cancer without evidence of metastatic disease. Still, initially undetected metastases are often not found until ^{131}I remnant ablation and a posttherapy whole-body scan are performed. The aim of this retrospective study was to determine whether ^{131}I-avid metastatic tumors are associated with a significant therapeutic (tumoricidal) ^{131}I effect after preparation of patients with rhTSH stimulation.

METHODS

Study Subjects

The study subjects were identified from 394 patients with differentiated thyroid cancer who had RRA at the Memorial Sloan-Kettering Cancer Center from 1997 through 2005. From this group of 394 patients, a total of 84 (21%) patients who had ^{131}I uptake in the thyroid bed and well-differentiated papillary or follicular thyroid cancer without known distant metastases at the time of RRA were included in the study. Excluded were patients with known or suspected distant metastases and with known residual gross tumor in the neck, and patients with interfering antithyroglobulin (Tg) antibodies (TgAb).

None of the 84 patients had palpable locoregional tumors at the time of RRA, and cross-sectional imaging studies were not routinely performed at the time of RRA in patients with ^{131}I-avid disease in the neck. However, chest computed tomography (CT) scans were performed in all patients who had ^{131}I-avid uptake in the lungs, which permitted structural correlations in patients with pulmonary uptake on the postablation RRA scans, but not confined to the neck.

RRA Preparation

All patients had near-total thyroidectomy prior to RRA and all were instructed to follow a low-iodine diet for at least 1 week prior to ablation.

RESULTS

Patient Characteristics (Figures 1 and 2)

The study identified 84 patients with ^{131}I-avid metastatic tumors localized outside the thyroid bed either on the initial ^{131}I diagnostic scan (DxWBS) (63 of 84, 75%) or only on the posttherapy ^{131}I scan (RxWBS) (21 of 84, 25%) all of which were visualized on both the DxWBS and the RxWBS. Of the 84 patients, 64 (76%) were prepared for RRA with rhTSH stimulation (rhTSH–RRA) and 20 (24%) were prepared with thyroid hormone withdrawal (THW–RRA). Most of the patients (81%) had an rhTSH-positive DxWBS 12 to 18 months after RRA. Patient age, sex, cancer histology, clinical TNM (tumor–node–metastasis classification), and tumor stage was not

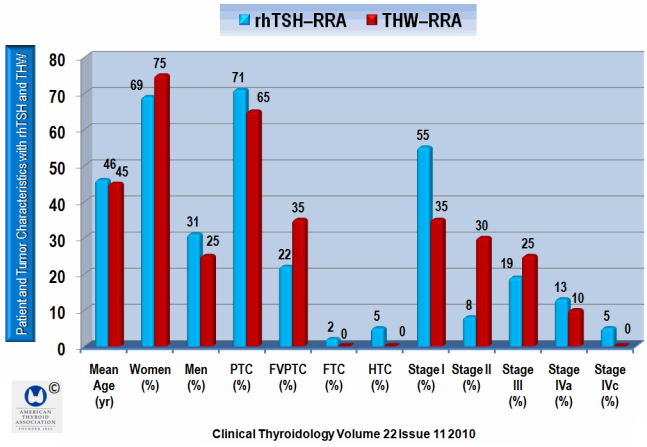

Figure 1. This figure shows the patient and tumor characteristics.
FTC = follicular thyroid carcinoma; FVPTC = follicular variant papillary thyroid carcinoma; HTC = Hürthle cell carcinoma; PTC = papillary thyroid carcinoma; RRA = radioiodine remnant ablation; rhTSH = recombinant human thyrotropin; THW = thyroid hormone withdrawal. This figure and Figures 2 and 3 are derived from Table 1 of Tuttle et al.

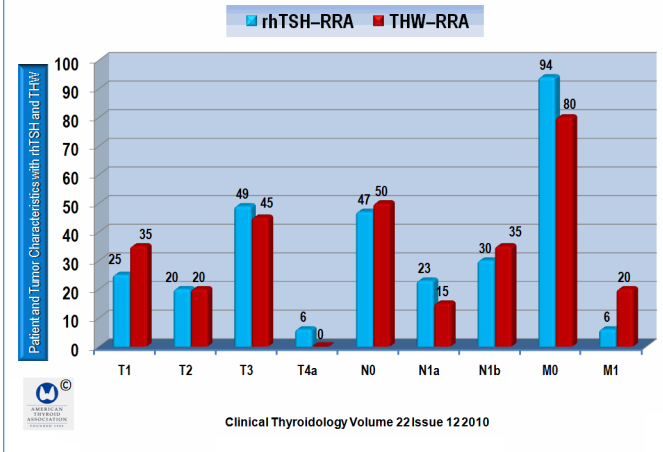

Figure 2. This is a continuation of Figure 1. The figure shows the TNM (tumor–node–metastasis staging system.
RRA = remnant ablation;
rhTSH = recombinant human thyrotropin;
THW = thyroid hormone withdrawal.
TNM = tumor–node–metastasis.

statistically different between the rhTSH and THW groups (Figures 1 and 2). All patients were initially thought to be M0 (no distant metastases) prior to RRA, but after the findings of ^{131}I-avid distant metastases during RRA, the TNM diagnosis was upgraded in 8 patients to M1 (distant metastases present), of which 4 were in the rhTSH–RRA group and 4 in the THW–RRA group. The median administered ^{131}I activity was 144 mCi in the rhTSH–RRA group and 108 mCi in the THW–RRA group (P = 0.307). The ^{131}I-avid disease was initially detected on the DxWBS in most of the patients (75% of the rhTSH–RRA group vs. 90% in the THW–RRA group; P = 0.2).

Patients in both groups had RRA-avid tumor identified mainly as locoregional metastases alone (rhTSH–RRA, 60 of 64, 94%; THW–RRA, 16 of 20, 80%). The remaining patients had lung metastases alone or with both locoregional and lung metastases. The clinical outcomes were determined a median of 2.7 years after RRA.

Clinical Outcomes (Figure 3 and 4)

Although ^{131}I-avid metastatic tumors were identified outside the thyroid bed at the time of initial ablation, 45 of 64 (70%) of the rhTSH–RRA group and 11 of 20 (55%) of the THW–RRA group were rendered NED (no evidence of disease) a median of 2.7 years after the initial ^{131}I–RRA (P = 0.159) (Figure 2). Persistent disease was found in 19 of 64 patients(30%) following rhTSH–RRA and in 9 of 20 (45%) following THW–RRA (Figure 3). Cross-sectional imaging performed on all patients identified 5 of 19 (26%) in the rhTSH–RRA group and in 4 of 9 (44%) in the THW–RRA group with persistently abnormal Tg values during follow-up. Also, 1 patient in the rhTSH–RRA group also had non-^{131}I-avid lung metastases and ^{131}I-avid mediastinal lymph-node metastases (Figure 4).

An undetectable stimulated serum Tg <0.6 µg/L 12 to 18 months after RRA was achieved in 28 of 64 (44%) of the rhTSH–RRA group as compared with 6 of 20 (30%) of the THW–RRA group (P = 0.20). If the definition of NED was changed to an undetectable stimulated serum Tg value, 25 of 64 (39%) of the rhTSH–RRA group and 5 of 20 (25%) of the THW–RRA group would be classified as NED 12 to 18 months after initial RRA (P = 0.19) (Figure 4).

^{131}I-Avid Lesions Identified by DxWBS Prior to RRA

(Figures 5 and 6, on next page)

Concerning the outcome of ^{131}I-avid lesions identified on the DxWBS studies prior to RRA, 48 in the rhTSH–RRA group and 18 in the THW–RRA group, follow-up rhTSH-stimulated DxWBS identified persistent tumor in the same locations in 9 of 48 (19%) of the rhTSH–RRA group and 0 of 18 of the THW–RRA group (P = 0.1). However, new sites of ^{131}I-avid tumors were detected on the follow-up rhTSH-stimulated DxWBS in 1 of 48 (2%) of patients in the rhTSH –RRA group (with new uptake in the neck, and 1 patient with new uptake in the lungs), and 2 of 18 (11%) in the THW–RRA (1 patient with new uptake in the neck and 1 with new uptake in the lungs (P = 0.17) (Figure 6).

In the rhTSH–RRA group, identifiable tumor was associated with a stimulated Tg >2 µg/L in all five cases and a positive diagnostic DxWBS in one case. In the THW–RRA group, three of the four cases with structurally identifiable disease had a stimulated serum Tg >2 µg/L, and two of the cases had a positive DxWBS.

Among the patients classified as having persistent disease on the basis of a follow-up DxWBS, the site of persistent ^{131}I uptake was correlated with the site of uptake on the initial preablation diagnostic scan in 11 of 12 patients (92%). One patient in the rhTSH–RRA group had new uptake in a mediastinal lymph-node metastasis, not seen on preablation ultrasonography.

CONCLUSION

Preparation with rhTSH or THW stimulation has a similar therapeutic (tumoricidal) effect on small-volume metastatic disease discovered incidentally at the time of remnant ablation.

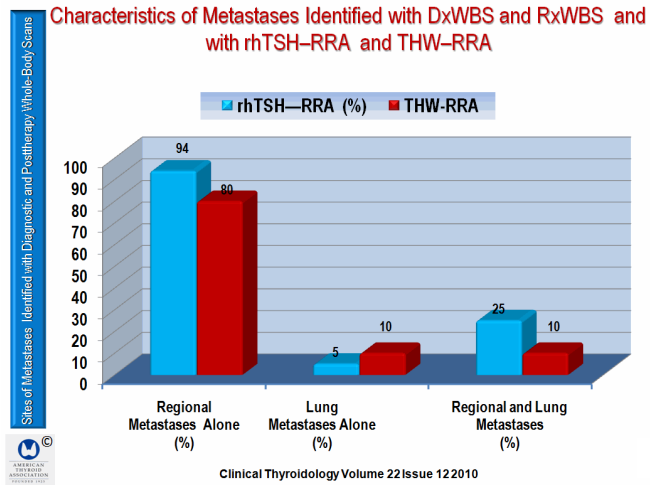

Figure 3. This figure shows the characteristics identified with diagnostic whole-body scans (DxWBS) and posttherapy whole-body scans (RxWBS). TNM = tumor–node–metastasis.

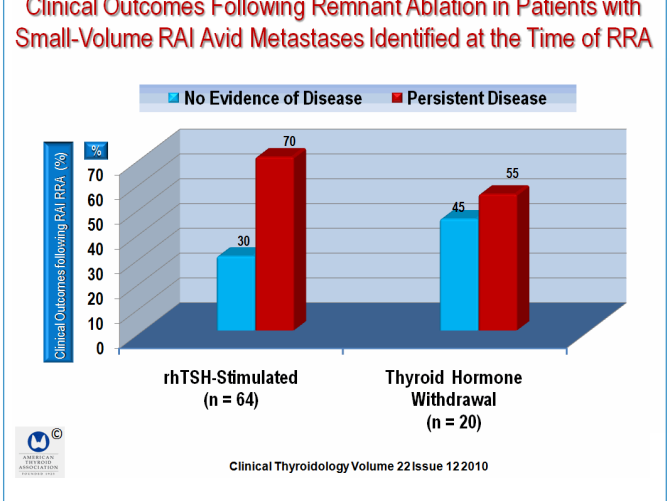

Figure 4. This figure shows the clinical outcomes following radioiodine remnant ablation (RRA) in patients with small-volume ^{131}I-avid metastases identified at the time of RRA. This figure is derived from Figure 1 of Tuttle et al.

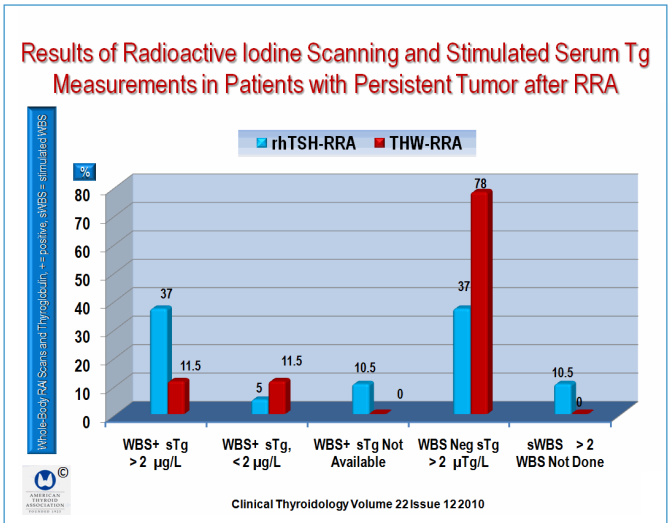

Figure 5. This figure shows the results of ^{131}I scanning and stimulated serum Tg measurements in patients with persistent tumor after RRA. This figure is derived from Table 2 of Tuttle et al. RAI = radioactive iodine; RRA = radioiodine remnant ablation; rhTSH = recombinant human thyrotropin; sTg = stimulated serum Tg. sWBS = stimulated whole-body scan; THW = thyroid hormone withdrawal; WBS = whole-body scan.

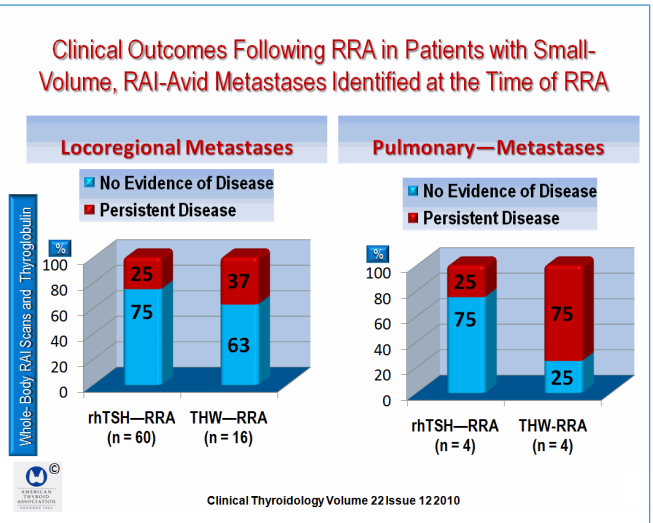

Figure 6. This figure shows the clinical outcomes based on the site of ^{131}I metastatic disease. Similar adjuvant therapy effects were observed in locoregional metastases in both rhTSH–RRA and THW–RRA. RAI = radioactive iodine; RRA = radioiodine remnant ablation; rhTSH = recombinant human thyrotropin; sTg = stimulated serum Tg. sWBS = stimulated whole-body scan; THW = thyroid hormone withdrawal.

COMMENTARY

This study demonstrates the concept that the first treatment with ^{131}I following total thyroidectomy for thyroid cancer has both an ablative and adjuvant therapy (tumoricidal) function. Tuttle et al. found that rhTSH-stimulated ^{131}I ablation resulted in successful adjuvant therapy in 70% of the patients when ^{131}I-avid metastatic tumors were first found at the time of remnant ablation, as compared with 55% of patients prepared with THW (P = 0.159).

Tuttle et al. point out that the data in this study are consistent with the earlier reports of successful adjuvant therapy of incidentally discovered ^{131}I-avid metastases with rhTSH preparation (1). However, Tuttle suggests that the relatively high rates of successful adjuvant therapy are probably largely related to the entry criteria in this study, and that only patients with small-volume ^{131}I-avid metastases would have been included in this study, which might be expected (2).

This is an important study, but Tuttle et al. warn that this treatment may not be effective when macrometastases are present.

— Ernest L. Mazzaferri, MD, MACP

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1. Pilli T, Brianzoni E, Capoccetti F, et al. A comparison of 1850 (50 mCi) and 3700 MBq (100 mCi) 131-iodine administered doses for recombinant thyrotropin-stimulated postoperative thyroid remnant ablation in differentiated thyroid cancer. J Clin Endocrinol Metab 2007;92:3542-6.

2. 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.

Pregnancy may not have an impact on tumor recurrence in women with differentiated thyroid cancer

Hirsch D, Levy S, Tsvetov G, Weinstein R, Lifshitz A, Singer J, Shraga-Slutzky I, Grozinski-Glasberg S, Shimon I, Benbassat C. Impact of pregnancy on outcome and prognosis of survivors of papillary thyroid cancer. Thyroid 2010;20:1179-85. 10.1089/thy.2010.0081 [doi]

SUMMARY

BACKGROUND

Thyroid cancer affects women more often than men by a ratio of almost 3 to 1. Moreover, papillary thyroid cancer (PTC) is the most common form of differentiated thyroid cancer (DTC) among women of childbearing age, 10% of whom are either pregnant or are in the early postpartum period when thyroid cancer is diagnosed. Although the prevalence of thyroid cancer in pregnant women remains high, most are first identified after delivery. Still, the management of thyroid cancer during pregnancy poses serious diagnostic and therapeutic challenges to both the patient and the fetus. The thyroid gland may secrete more thyroid hormone than usual during early pregnancy, which some suggest may not only be the cause of this problem, but might also be responsible for the higher rate of DTC during pregnancy. There is concern about therapy for thyroid cancer during this period, mainly the timing of surgery, the use of levothyroxine, and the assessment of follow-up during gestation. The aim of this study was to determine whether pregnancy in thyroid cancer survivors poses a risk of progression or recurrence of thyroid cancer.

METHODS

This retrospective study comprises a group of consecutive women who had follow-up at the Endocrine Institute of Rabin Medical Center in Tel Aviv, Israel, for PTC from 1992 through 2009 who gave birth at least once after receiving thyroid cancer therapy. Medical records were reviewed for age at the time of thyroid cancer diagnosis and the age at delivery, tumor pathology, lymph-node metastases, and tumor–node–metastases (TNM) tumor staging according to the American Joint Committee on Cancer (6th edition) and the type of treatment, including thyroidectomy, lobectomy, and radioactive iodine (^{131}I); repeated surgeries and repeated ^{131}I treatments; levels of thyroglobulin (Tg) before and during pregnancy and 1 year after delivery; and thyrotropin (TSH) levels during pregnancy.

Thyroid cancer status before pregnancy was categorized as follows: free of disease, defined as a Tg level <0.9 ng/ml on levothyroxine (L-T_4) therapy with negative anti-Tg antibodies (TgAb) and negative neck ultrasonography; or persistent tumor defined by at least one of the following—Tg >0.9 ng/ml on L-T_4 therapy, neck mass on imaging studies with positive cytology for thyroid cancer metastases, or radioiodine uptake outside the thyroid bed and persistent TgAb that increased over time. The following features that were used to determine thyroid cancer progression or recurrence during pregnancy and postpregnancy within 1 year after delivery were Tg levels during L-T_4 therapy, neck ultrasonography, and TgAb titers during follow-up.

Progression of thyroid cancer during pregnancy was defined as one or more of the following: a 20% or larger increase in serum Tg from the prepregnancy level or a consistent increase of 20% or more in serum TgAb levels during pregnancy, new metastatic tumors on neck ultrasonography performed within 1 year after delivery, or an increase in size of a prepregnancy tumor on neck ultrasonography. Persistent disease before conception and the presence or absence of disease progression during pregnancy was analyzed against the demographic parameters, and disease-related indexes, such as TSH levels during pregnancy. All pregnancies were included in the analysis.

RESULTS

Clinical Characteristics (Figures 1 to 3)

A total of 63 women satisfied the inclusion criteria for the study. All were younger than 45 years of age at the time of diagnosis of thyroid cancer (Figure 1). Treatment comprised total thyroidectomy in 59 women, 58 of whom (98.3%) had thyroid remnant ablation (RRA), whereas hemithyroidectomy was performed in 4 women, none of whom had RRA. A total of 40 women gave birth to 90 children. The mean (±SD) duration from the time of treatment to the first delivery was 5.08±4.39 years (median, 3.20) and the mean duration of follow-up after the first delivery was 4.84±3.80 years (range, 3 to 17.3; median, 3.75). The demographic, clinical, histopathological, and biochemical features of the patients during the first pregnancy are shown in Figures 1, 2, and 3.

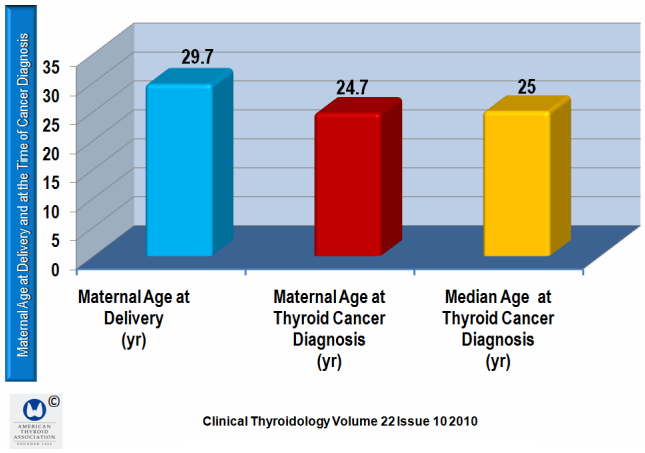

Figure 1. Figures 1, 2, and 3 show the demographic, clinical, histopathological, and biochemical features in 63 women who were thyroid cancer survivors. This figure shows the median age at the time of delivery, the maternal age at the time of diagnosis, and the median age at the time of cancer diagnosis. The first three figures were derived from data in Table 1 of Hirsch et al.

Persistent Tumor before the First Pregnancy (Figure 4)

Thirteen of the 63 women (20.6%) had persistent PTC before conception. Their serum Tg levels and imaging findings before and after pregnancy are shown in Figure 4. Five women had lymph-node dissection after initial surgery before conception, and 12 had persistent disease on the basis of a detectable serum Tg levels on L-T_4 therapy with or without imaging studies. One patient conceived 3 months after RRA and did not have neck ultrasonography or Tg measurements after delivery when lymph-node metastases were detected.

Serum Thyroglobulin Levels (Figure 4)

All serum Tg levels were measured during L-T_4 therapy. Excluded from this group were 4 patients treated with hemithyroidectomy, and 7 who were positive for serum TgAb. Also excluded were 5 women in whom pertinent study data were missing.

Among the remaining 47 women, the mean Tg level before the first pregnancy was 1.23±3.93 ng/ml (range, 0 to 23.9), and the mean postpartum Tg level was 1.18±3.54 ng/ml (range, 0 to 21.4). The difference was not statistically significant. In 39 of the 47 women (82.9%), a Tg level <0.9 ng/ml was documented before and after the first pregnancy. The data for the other 8 women are shown in Figure 4. In a group of 8 patients, there were no changes in serum Tg levels before pregnancy and after delivery with a mean suppressed serum Tg of 7.42±7.37 ng/ml, and 7.01±6.44 ng/ml, respectively, with a serum TSH suppression level before pregnancy of 0.1±0.13 mIU/L after delivery.

Tg was detectable before and after pregnancy in 7 of 8 women, whereas in 1 patient the serum Tg was undetectable before pregnancy but increased postpartum to detectable levels of 1.7 ng/ml, which was considered to indicate progression of cancer during pregnancy. Only 1 patient among those with detectable serum Tg levels had undetectable serum Tg levels before pregnancy that increased during pregnancy as the result of lymph-node metastases that were detected 5 months postpartum.

Structural Evidence of Tumor (Figure 3)

For 56 women in whom ultrasound data were available, 50 (89%) had negative ultrasound studies, whereas 4 of the remaining 6 women had fine-needle aspiration biopsy that revealed PTC cytology and 2 had ^{131}I uptake outside the thyroid bed. In 2 of the 6 women, the serum Tg level before pregnancy was <0.9 ng/ml on L-T_4 therapy, and in 1 patient the serum Tg levels were unavailable.

None of the patients with normal prepregnancy neck ultrasonography had new abnormal ultrasound findings after delivery. However, of the 6 women with abnormal prepregnancy neck ultrasound findings, 1 had new lymph-node metastases 5 months postpartum and another had growth of a preexisting malignant lymph node 3 months postpartum.

Serum TSH during the First Pregnancy

After the first diagnosis of DTC during pregnancy in 58 of 63 women (92%), 52 (89%) had their first TSH measurement performed in the first trimester; the remaining 6 had their first TSH measurement in the second trimester. In most of the women, the serum TSH level was measured a median of five times during pregnancy, during which the mean values were 2.65±4.14 mIU/L (median, 1.20), and only 8 (12.6%) had TSH levels <1 mIU/L throughout the first pregnancy. Still, there was no correlation between serum TSH levels and disease progression or Tg level during pregnancy.

Progression of Thyroid Cancer during Pregnancy (Figure 4)

Progression of thyroid cancer was considered to be present in 6 of 63 patients (9.5%) during their first pregnancy after diagnosis of thyroid cancer. In 4 patients, this was based on a new finding or worsening of a preexisting finding on neck ultrasonography within a year after delivery combined with a positive cytology for PTC, in another patient it was based on a postpartum elevation of serum Tg levels, and in another it was based on a consistent increase in serum TgAb levels throughout the follow-up period, including pregnancy (Figure 5).

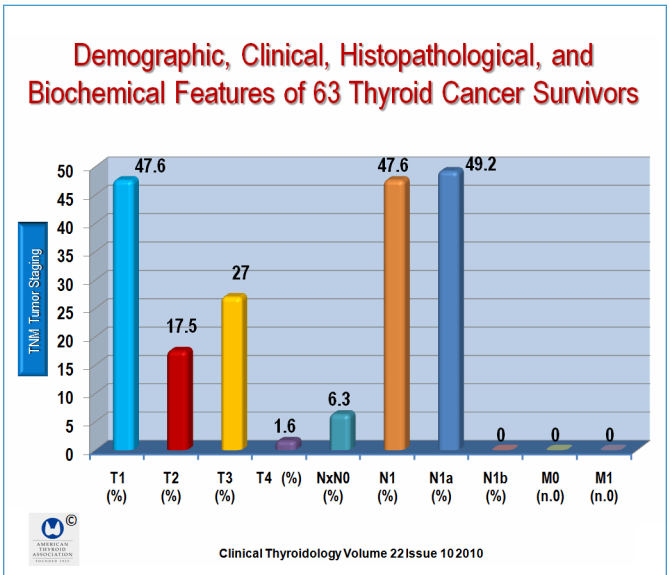

Figure 2. This figure shows the tumor–node–metastasis (TNM) features of the 63 pregnant patients with thyroid cancer.

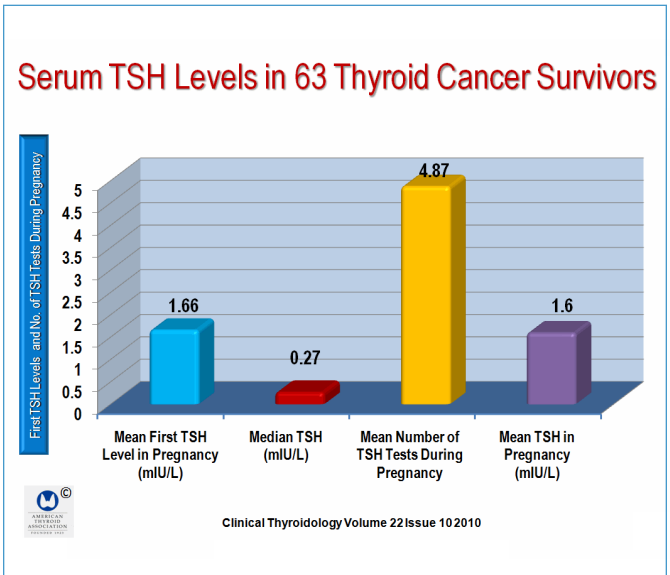

Figure 3. This figure shows the serum thyrotropin (TSH) levels in the 63 pregnant women who were thyroid cancer survivors.

Correlation of Clinical Factors with Disease Persistence during Pregnancy (Figures 4 and 5)

The persistence of thyroid cancer before pregnancy was correlated with tumor size, tumor extension, and TNM staging (P = 0.001, r = 0.345). It was also correlated with the total amount of ^{131}I administered until conception and during the follow-up period: women with persistent tumor before pregnancy were treated with 99.7±69.23.63 mCi; the mean total during the entire follow-up was 345.8±109 mCi in the women with persistent disease and 115.4±87 mCi in women with no prepregnancy evidence of disease (P<0.001, r = 0.729). In addition, disease persistence was also correlated with serum Tg levels before pregnancy (P<0.001, r = 0.606). No significant correlation was found between disease persistence and the other parameters measured.

There also was no correlation with patient age at diagnosis of thyroid cancer; patient age at delivery; interval from diagnosis of thyroid cancer to pregnancy; TNM staging; mean, median, or maximal TSH level during pregnancy; and Tg level before conception. However there was a strongly positive correlation between persistence of thyroid cancer before pregnancy and cancer progression during pregnancy (P<0.001). Every one of the 6 patients with progression of thyroid cancer during pregnancy had evidence of PTC persistence before conception. There also was a strong correlation between the total amounts of ^{131}I administered both until pregnancy and during the whole follow-up period with thyroid cancer progression during pregnancy. The total amount of ^{131}I administered until conception was 260±161.19 mCi in the women with PTC progression and 123±161 mCi in women without tumor progression (P = 0.003; r = 0.376). The total amount of ^{131}I during the whole follow-up period was 315.83±125.3 and 157.5±126.68 mCi, respectively (P = 0.005).

Progression of Thyroid Cancer during Second Pregnancy

A total of 23 women gave birth two times or more after thyroid cancer treatment, and thyroid cancer progressed during the second pregnancy in three women. These patients had persistent disease before both the first and the second pregnancies. Thyroid cancer progressed during both the first and second pregnancies in one woman, and only during the second pregnancy in two. Four women gave birth to three children after the diagnosis and treatment of PTC.

Current Patient Status

Of the 13 patients categorized as having persistent disease, 11 still had biochemical evidence of tumor with or without structural evidence of PTC at last follow-up and 6 were treated with additional therapy since giving birth. Two had dissection of lymph-node metastases, and another received an additional 150 mCi of ^{131}I and three others had surgery and received and additional 150 to 350 mCi of ^{131}I postpartum and have no evidence of disease.

CONCLUSION

Pregnancy may not have an impact on tumor recurrence in women with DTC.

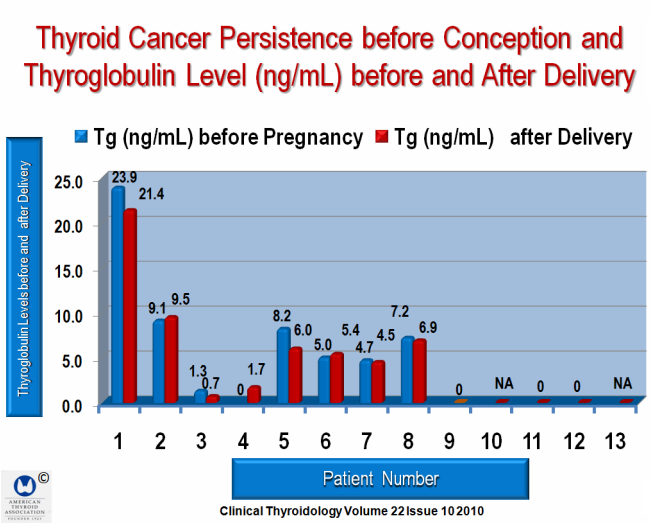

Figure 4. This figure shows the thyroid cancer persistence before conception and thyroglobulin levels before and after delivery. NA = not available.

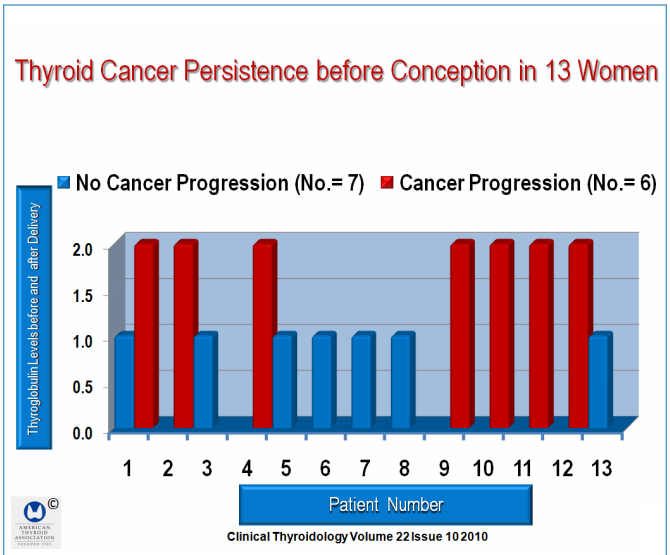

Figure 5. This figure shows thyroid cancer persistence before conception in 13 women, showing women with and without cancer progression

COMMENTARY

Thyroid cancer is a common problem in pregnant women. A study by Smith et al. (1) of almost 5 million obstetric deliveries in California from 1991 through 1999 found that nearly 5000 were pregnant women with invasive malignancy, comprising approximately 1 in 1000 births. There were 23 different types of cancer in these pregnant women, most of whom were diagnosed within a few months before or at the time of delivery. The two most common cancers were cancer of the breast (19 per 100,000) and thyroid cancer (14 per 100,000). About 25% were thyroid cancers identified prenatally, 2% were found at the time of delivery, and 75% were discovered during the postpartum period. The timing of the cancer diagnosis thus affected the clinical outcomes. The most favorable perinatal cancer outcomes occurred in women whose cancer diagnosis was made 6 to 9 months after delivery, comprising 6% of the cases, whereas the most unfavorable perinatal cancer outcomes were associated with thyroid cancer diagnosed 0 to 3 months before delivery. For women whose cancer was diagnosed postpartum, perinatal outcomes were thus minimally affected by the presumed existence of occult cancer at the time of obstetric delivery.

There has been some concern that female hormones are the cause of the high rate of thyroid cancer during pregnancy, which in some cases may be more aggressive tumors. Still, ionizing radiation remains the best-established risk factor for thyroid cancer (2), although other factors may be responsible for the high rate of thyroid cancer in women, particularly the thyroid-stimulating effects of human chorionic gonadotropin (HCG) and estrogen (3). Thyroid glands may secrete more thyroid hormone than usual during early pregnancy in response to HCG that overrides the normal operation of the hypothalamic–pituitary–thyroid feedback axis (4), effects that might be responsible for the high rates of thyroid cancer in pregnant women. However, the data concerning the effect of estrogens on thyroid cancer are conflicting (5,6), and the effects tend to be small (7).

During normal pregnancy, the stimulatory effects of HCG and estrogen produce changes in serum TSH, free thyroxine (FT_4), and FT_4 index and serum Tg concentrations during the third trimester that are substantially higher (by approximately 25%) than postpartum and second-trimester concentrations (8,9). There is a suggestion that estrogens may increase the expression of the Tg gene, increasing the potential production of Tg in DTC without stimulating the c-myc proto-oncogene and therefore not promoting rapid cell proliferation (10).

Hirsch report the serum Tg levels in pregnant women; however, the accuracy of serum Tg levels during pregnancy has been questioned in a number of studies, most of which have simultaneously evaluated serum thyroid hormone levels, FT_4, triiodothyronine (T_3) thyroid-binding globulin, and serum Tg. However, each of the studies has reached slightly differing conclusions.

One of the early studies of Tg during pregnancy was published in 1984 by Nakamura et al. (11), in which Tg levels in 52 women in various stages of pregnancy were compared with Tg in 15 age-matched nonpregnant women. Among the pregnant women, the mean serum Tg levels were 8.4 ng/L in the first trimester, 9.2 in the second, 10.1 early in the third trimester, and 12.1 late in the third trimester, as compared with a mean serum Tg of 6.0 ng/L in nonpregnant women. Still, the authors concluded that Tg levels in pregnant women could be clinically interpreted without regard to the coexistence of pregnancy.

A study in 1986 by Hara et al. (12) found that serum T_3, T_4, FT_4, thyroid-binding globulin, TSH, and Tg levels were all decreased in the third trimester as compared with the first trimester and with values in healthy nonpregnant individuals ($P<0.01$); nonetheless, serum TSH levels were higher than normal in all stages of pregnancy, with a significant rise in the third trimester that the authors attributed to the presence of a subclinical hypothyroid state in the late stage of normal pregnancy.

A study by Soldin et al. (8) found that trimester-specific T_3, FT_4, TSH, and Tg concentrations were significantly different in the first and third trimesters ($P<0.05$); however, in the second and third trimesters, FT_4, TSH, and Tg values were not significantly different, whereas T_3 was significantly higher in the third trimester as compared with the second trimester, but T_4 was not significantly different among any of the trimesters. Lastly, a clinical study by Leboeuf found that serum Tg levels in pregnant women may be high without detectable tumor (13).

The main finding of the study by Hirsch et al. is that pregnancy does not have an impact on tumor recurrence in women with differentiated thyroid cancer. A study by Moosa and myself (14) of 61 pregnant women showed no increased risk for tumor recurrence, distant recurrence, and cancer mortality as compared with age-matched controls.

Not mentioned in the Hirsch study is the outcome of pregnancy and fetal survival in this group of women who were initially treated with relatively large amounts of ^{131}I. Managing thyroid cancer in pregnant women involves therapeutic decisions for both the mother and fetus, including decisions concerning breast-feeding, subsequent pregnancies, and outcome of the fetus.

— Ernest L. Mazzaferri, MD, MACP

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Postablation Tg concentration predicts disease recurrence in patients with low-risk differentiated thyroid cancer

Pelttari H, Valimaki M, Loyttyniemi E, Schalin-Jantti C. Post-ablative serum thyroglobulin is an independent predictor of recurrence in low-risk differentiated thyroid carcinoma: a 16-yr follow-up study. Eur J Endocrinol 2010;163:757-63. EJE-10-0553 [pii];10.1530/EJE-10-0553 [doi]

SUMMARY

BACKGROUND

The incidence of differentiated thyroid cancer has been increasing steadily for the past several decades, especially the incidence of papillary thyroid cancer (PTC) and, to a lesser extent, follicular thyroid cancer (FTC). The prognoses of PTC and FTC are particularly favorable, with 5- and 10-year survival rates of 90% and 95%, respectively, when patients are properly treated. The tumor–node–metastasis (TNM) staging system is the most widely used means of predicting survival. Still, recurrence rates for these tumors are relatively high, ranging from 35% to 50%, depending on the patient's age and tumor characteristics, which are not reliably identified by the TNM staging system. The retrospective study by Pelttari et al. is aimed at identifying the variables that predict tumor recurrence.

PATIENTS AND METHODS

The study subjects are individuals treated at the Helsinki University Central Hospital (HUCH) district over a 15-year period from January 1, 1983, through December 31, 1997. The study subjects were selected from the clinical records of 710 patients (571 women and 139 men), 495 (70%) of whom comprised the final study group of patients with TNM stage I or II PTC or FTC and were considered free of disease and in complete remission after surgery and thyroid remnant ablation (RRA). Follow-up data for this group were identified from the clinical records of the patients.

Follow-up

To verify the current patient status, a questionnaire concerning the recent follow-up of thyroid cancer was also sent to patients whose documents revealed no recent entries. An 11.6-year follow-up of the cohort was described previously. The current study assessed recurrences and cancer-specific mortality in the cohort of 495 patients after a median follow-up of 16 years, in which prognostic factors for disease recurrence were evaluated, including patient age, sex, primary tumor size, tumor infiltration at the time of initial surgery, and lymph-node metastases and postablation serum thyroglobulin (Tg) concentrations.

Thyroglobulin

Postoperative Tg concentrations were obtained 4 to 6 weeks after surgery, and post-RRA Tg measurements were performed in combination with a ^{131}I whole-body scan 4 to 6 months after the first RRA, which was performed under thyrotropin (TSH) stimulation induced by levothyroxine (L-T_4) withdrawal. Serum Tg was measured by an ^{131}I kit with a detection limit of 3 µg/L until 1989, after which Tg was measured by an immunometric assay with a detection level of 1 µg/L. Anti-Tg antibody (TgAb) was evaluated with a ≥80% recovery.

Study Variables

Disease recurrence was defined as new evidence of tumor after a 12-month period without verification of disease, which included all tumor sites reported and confirmed either by imaging studies or surgery. Disease-free outcome was defined as an undetectable Tg, with no clinical evidence of disease and no radiologic evidence of tumor. Clinical and histologic variables included in the study were tumor size, the presence of lymph-node metastases, locoregional infiltration of tumor, and completeness of surgery as estimated by the surgeon performing the procedure. Local tumor infiltration was defined as macroscopic adherence of tumor into the adjoining muscle or soft tissue or microscopic invasion of adjoining tissue. The biologic variables were Tg concentrations measured after surgery and after RRA and measurement of TgAb.

RESULTS

Patient Features and Initial Therapy

The study cohort comprised 415 women (83.8%) and 80 men (16.2%), with a mean age at diagnosis of 40.6 years. A total of 461 tumors were PTCs (93.1%) and 31 were FTCs (6.1%). Mean tumor size was 1.8 cm (range, 0.3 to 6.0); FTCs were larger than PTCs (mean, 3.0 vs. 1.6 cm; P = 0.16). Tumor was classified in 13 patients as TNM pT3 due to tumor size.

Initial Surgery

Primary surgery was total or near-total thyroidectomy in 448 (95%) of the 472 patients. Locoregional lymph-node metastases were found in 59 of the 472 patients (12.5%). Although systematic lymph-node dissection was not performed, patients with lymph-node metastases detected before or during surgery had lymph-node surgery. At initial surgery, locoregional tumor infiltration was detected in 37 patients (7.4%) and surgery was complete in all but 3 of 472 (0.6%) patients.

Thyroid Remnant Ablation

Of the 472 patients, 414 (87.7%) had RRA followed by repeat ^{131}I therapy as necessary. The median RRA ^{131}I activity administered was 3.7 GBq (100mCi; range, 2.2 to 25.9 [100 to 700 mCi]).

Criteria for Classifying Patients as Free of Disease

Patients were considered to be free of disease if the neck ultrasound (US) examination was negative, serum Tg was unmeasurable after L-T_4 withdrawal, and there was no uptake on a diagnostic whole-body scan. One patient had distant metastases at the time of diagnosis and was classified as TNM stage II on the basis of her young age. All patients had follow-up of at least 10 years (range, 10 to 24) with a median follow-up of 16 years.

Tumor Recurrence

A total of 51 of the 472 patients (10.8%) had a tumor recurrence. Five of the 51 (10%) had FTC and 46 (90%) had PTC. A total of 43 (84.3%) of the detected recurrences were identified within 10 years from the time of initial diagnosis and therapy. The majority of recurrences (94.1%) were cervical-lymph-node metastases, 54.9% of which were detected with neck ultrasound and confirmed by tumor histology. A smaller number of recurrences (31.4%) were confirmed with new ^{131}I uptake on a diagnostic whole-body scan. Two patients required more therapeutic ^{131}I because of a significant increase in serum Tg on L-T_4 therapy without radiologic findings of tumor. This was confirmed by a posttreatment ^{131}I whole-body scan (RxWBS). In one case each, recurrence was detected on the basis of an increase serum Tg concentration on L-T_4 therapy, combined with palpable lymph nodes and suspicious ultrasound findings, and the appearance of TgAb was indicated by a declining Tg recovery. Thyroid cancer was the cause of death in one patient who had FTC that metastasized at a young age.

Postsurgical Thyroglobulin and Tumor Recurrence

Postsurgical serum Tg levels were found in 468 (94.5%) of the 472 patients. After primary near-total or total thyroidectomy, 250 of 472 patients (52.9%) had postsurgical serum Tg levels greater than the detection limit. A total of 34 of the 51 patients with disease recurrence had a postoperative Tg above the detection limit, as compared with 225 (54%) of the 420 patients without tumor recurrence (P = 0.251). There was no correlation between postoperative Tg and serum TSH levels. Median postoperative TSH concentration (76 and 73 mIU/L) did not differ among patients with and without recurrence, respectively (P = 0.39).

Serum Thyroglobulin levels after Thyroid Remnant Ablation and Disease Recurrence (Figure 1)

RRA was performed in 413 of the 472 patients (97%) who had total or near-total thyroidectomy (49 patients with recurrence and 364 without recurrence) (Figure 1). Post-RRA Tg levels were found in 401 patients (96.6%) and were detectable after the first RRA in 51 patients (12.7%; median, 10.0 µg/L [range, 1 to 500]). All patients with detectable Tg after RRA were treated with repeated amounts of ^{131}I until Tg became undetectable on RxWBS. The amount of ^{131}I administered ranged from 2.2 to 25.9 GBq (60 to 700 mCi). After RRA, Tg was detectable in 36.4% of patients with subsequent recurrence as compared with 9.8% without recurrence (P<0.0001). Median TSH concentrations of corresponding thyroid post-RRA were 44 and 36 mIU/L, respectively (P = 0.021). Of the 79 patients with undetectable serum Tg after RRA, a low recovery (<80%) was an indication of positive serum TgAb levels, and 9 of these patients had tumor recurrence.

Multivariate Logistic-Regression Analysis (Figure 2)

The independent predictors of disease recurrence were elevated postablation serum Tg concentrations, lymph-node metastases, and local tumor invasion (Figure 2).

CONCLUSION

Postablation Tg concentration is a robust predictor of disease recurrence in patients with differentiated thyroid cancer.

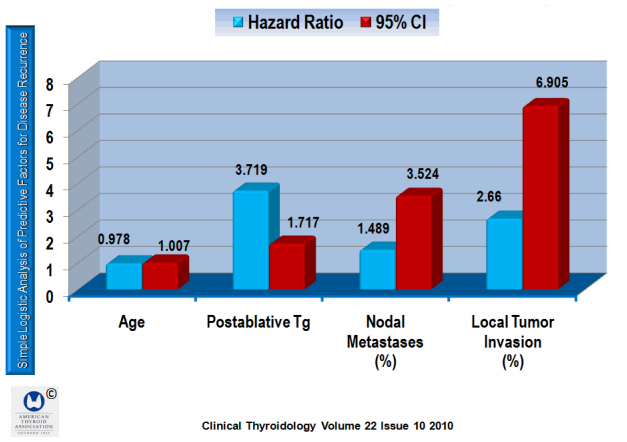

Figure 2. Figure 2 shows the independent variables, hazard ratio and 95% confidence intervals that identified the predictors of recurrence according to multivariate logistic regression analysis. CI = confidence interval.

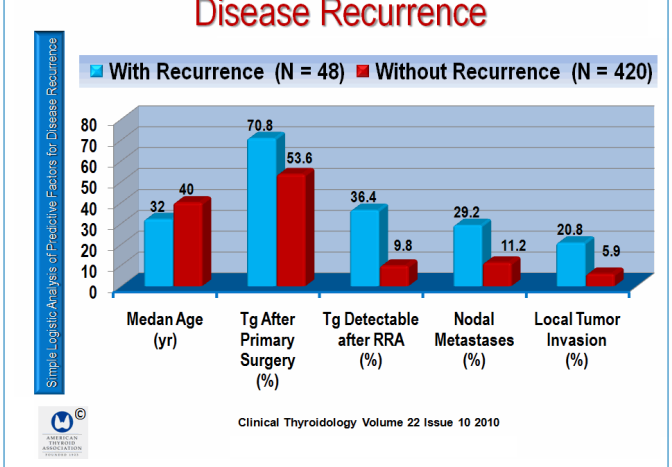

Figure 1. This figure shows the simple logistic analysis of predictive factors for disease recurrence. RRA = thyroid remnant ablation; Tg = thyroglobulin. This figure is derived from data in Table 2 of Pelttari et al.

COMMENTARY

The authors of this study initially reported the first set of data concerning the follow-up of this study cohort in 2008 (1) after a 5-year follow-up, during which the recurrence rate was 2.4%. However, after the current median follow-up of 11.6 years, the same study cohort of 495 patients at low-risk for thyroid cancer mortality found that one patient died of thyroid cancer and 51 patients had a nearly 11% (10.8%) rate of tumor recurrence. The authors point out that the recurrence rate has been steadily approaching that of the 14 to 15% reported after 30 years in a follow-up study from the Mayo Clinic (2). Pelttari et al. suggest that it is thus important to identify recurrence in this group of patients who may have recurrences many years after initial therapy. The authors found that tumor invasion at the time of initial surgery and detectable serum Tg concentrations after RRA (off L-T_4) were the only independent predictors of a late recurrence. This is particularly important, as the TNM classification fails to identify patients at risk for tumor recurrence.

Only a few studies have addressed this problem, showing that serum Tg levels at the time of RRA just after thyroidectomy are useful in predicting clinical recurrence in patients with low-risk tumors (3-5).

These studies underscore the importance of recurrence in patients with low-risk tumors, especially those with PTC and FTC and the utility of TSH-stimulated serum Tg levels within a short time after initial surgery has been performed.

— Ernest L. Mazzaferri, MD, MACP

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Tumor multifocality and extrathyroidal tumor extension should be considered for prophylactic CLND, especially in men with papillary thyroid microcarcinoma

So YK, Son YI, Hong SD, Seo MY, Baek CH, Jeong HS, Chung MK. Subclinical lymph node metastasis in papillary thyroid microcarcinoma: a study of 551 resections. Surgery 2010;148;526-31. S0039-6060(10)00013-9 [pii];10.1016/j.surg.2010.01.003 [doi]

SUMMARY

BACKGROUND

The frequency of subclinical lymph-node metastases (LNM) in the central cervical-lymph-node compartment may be found in up to 65% of clinically negative lymph-node metastases in papillary thyroid microcarcinomas (PTMC). However, routine prophylactic central-neck lymph-node dissection (CLND) continues to be a matter of debate, concerning both the efficacy of this surgical procedure and the possibility of parathyroid or recurrent laryngeal-nerve injury. The aim of this study was to assess the clinicopathologic factors associated with subclinical central lymph-node dissection and the recurrence rates and postoperative complications of total thyroidectomy and CLND.

PATIENTS AND METHODS

A total of 551 patients treated from 2005 through 2009 with clinically node-negative PTMC based on preoperative neck ultrasonography and fine-needle aspiration biopsy comprised the study subjects, all of whom had had total thyroidectomy and bilateral prophylactic CLND. The diagnosis of PTMC was reconfirmed by the surgical pathology findings for all patients.

RESULTS

Clinicopathologic Characteristics of the Study Patients (Figures 1 and 2)

The clinicopathologic characteristics of these patients are shown in Figure 1. A total of 440 women (79.9%) and 111 men (20.1%) comprise the study subjects, whose mean age was 50.2±9.2 years. The mean tumor size was 0.6±0.2 cm, and for multifocal tumors, the largest tumor was used in the analysis. The majority of patients (98.5%) had classic papillary thyroid cancer (Figure 2). The mean number of lymph nodes in the central compartment was 8.9 (range, 1 to 41), and the surgeon's description verified the adequacy of bilateral CLND, whereas patients who had unilateral CLND were excluded from the study. A total of 73.8% of the patients had bilateral CLND with PTMC.

Extent of Tumor (Figure 3)

The extent of tumor was classified into three categories based on the pathology results: confined within the capsule, capsule invasion (n = 11 patients, 2%), and extrathyroidal extension (n = 292, 53%). Extrathyroidal extension was mostly minimal invasion of perithyroidal soft tissue or strap muscle (pT3), which also included microscopic capsule invasion into perithyroidal tissue (Figure 3). Only 4 patients had invasion of tumor into the adjacent organs (pT4); all of which had posterior extension to the recurrent laryngeal nerve.

Postoperative Radioiodine (^{131}I) Treatment

Patients with unfavorable pathologic characteristics, such as multifocal tumors, extrathyroidal extension, angiolymphatic invasion, or lateral LNM were treated with ^{131}I. A total of 444 of 551 (80.6%) patients were treated with a mean and median of 42.6 and 30.0 mCi of ^{131}I, respectively. A total of

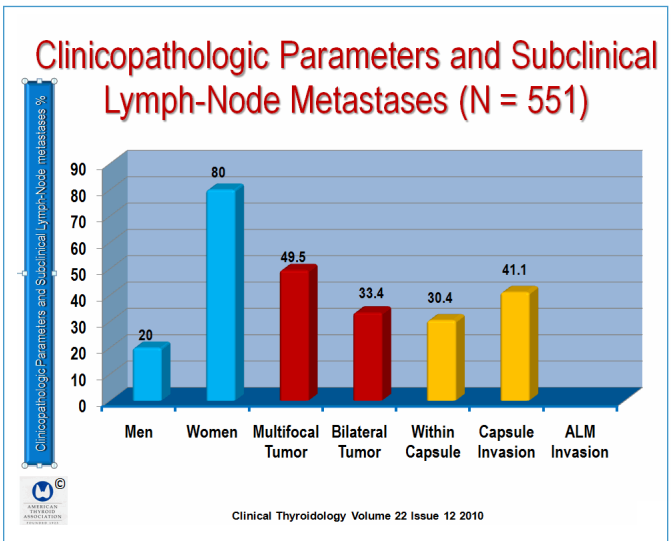

Figure 1. This figure shows the clinicopathologic and subclinical lymph-node metastases. The data for this figure are derived from Table 1 of So et al. ALM = Angiolymphatic invasion.

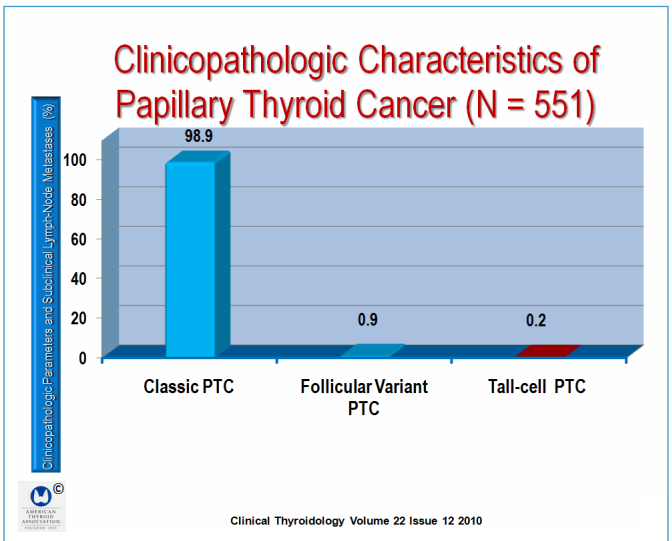

Figure 2. This figure shows the clinicopathologic characteristics in 551 patients. The data for this figure are derived from Table 1 of So et al.

242 patients (44.1%) had ≥2 ^{131}I treatments. The first ^{131}I treatment was performed within 2 to 3 months of surgery and was administered after 4 weeks of thyroid hormone withdrawal, with a TSH >30 mIU/L. Subsequent ^{131}I treatments were based on the serum Tg levels, anti-Tg antibody (TgAb), and the RxWBS. When ^{131}I was no longer required, patients had regular follow-up with ultrasonography and unstimulated serum Tg levels. Fine-needle aspiration was performed if pathologic confirmation of recurrence was necessary.

Complications

Postoperative hypocalcemia was defined as at least 1 event of hypocalcemic symptoms, including perioral numbness or hand and feet paresthesia, or at least of 1 ionized calcium level <1.0 mmol/L or a total calcium level <8.0 mg/dl.

Permanent hypocalcemia was defined as persistent symptoms or persistent biochemical hypocalcemia for more than 6 months. Postoperative vocal-cord palsy, chyle leakage, or hematoma was also investigated, and patients had monthly laryngoscopy at every follow-up regardless of corrective thyroplasty.

Central Lymph-Node Metastases

Among 551 patients with clinically node-negative PTMCs, subclinical central LNM was identified in 202 (36.7%). The mean number of metastatic lymph nodes was 2.4±1.9. The frequency of LNM was greater in men (P = 0.002), in patients with multifocal tumors (P = 0.003), and in patients with capsule invasion or extrathyroidal extension (P = 0.001). Tumor size >0.5 cm and angiolymphatic invasion were also associated with subclinical central LNM (P = 0.010 and 0.008, respectively) (Figure 1).

Multivariate analysis showed that the following were independently predictive of subclinical central LNM (odds ratio [OR], 2.184; P = 0.001), tumor multifocality, (OR, 1.582; P = 0.015), and extrathyroidal extension (OR, 1.893; P = 0.001). The probability that a woman with a solitary tumor confined within the thyroid capsule did not have central LNM was 80.6%, and the sensitivity and specificity were 38.6% and 85.6%, respectively (Figure 4).

Postoperative Complications

Transient hypocalcemia occurred in 152 patients (27.6%), in whom it resolved within 6 months. Permanent hypocalcemia developed in 6 patients (1.1%). Vocal-cord palsy developed in 28 patients, 21 of whom (3.8%) recovered within 6 months. Seven patients (1.3%) had vocal palsy that persisted for more than 1 year with permanent vocal palsy, and injection laryngoplasty was performed. Chyle leakage occurred in 3 patients (0.5%), and the rates of leakage were <100 ml/day in all cases. Leakage was controlled nonoperatively with a fat-free diet. A postoperative hematoma developed in 3 patients (0.5%) and was treated with reoperation.

Recurrence

Six patients were lost to follow-up (5.4%) and 104 had follow-up for more than 3 years after surgery. The median duration of follow-up was 40.5 months. There were no recurrences in the central cervical compartment (level VI), and only 1 patient had a recurrence outside the central cervical compartment (level IV) ipsilateral to the primary tumor 19 months after thyroidectomy. The 3-year locoregional control rate was 99.0%.

CONCLUSION

The frequency of subclinical central LNM was high in PTMC and was managed with prophylactic CLND, which did not cause permanent morbidity. PTMC multifocality and extrathyroidal tumor extension should be considered for prophylactic CLND, especially in men.

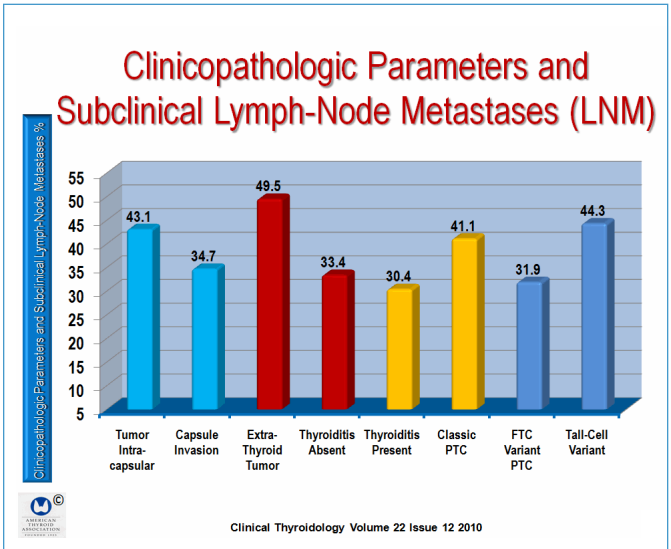

Figure 3. This figure shows the clinicopathologic parameters and subclinical lymph-node metastases (LNM).
FTC = follicular thyroid carcinoma;
PTC = papillary thyroid carcinoma.

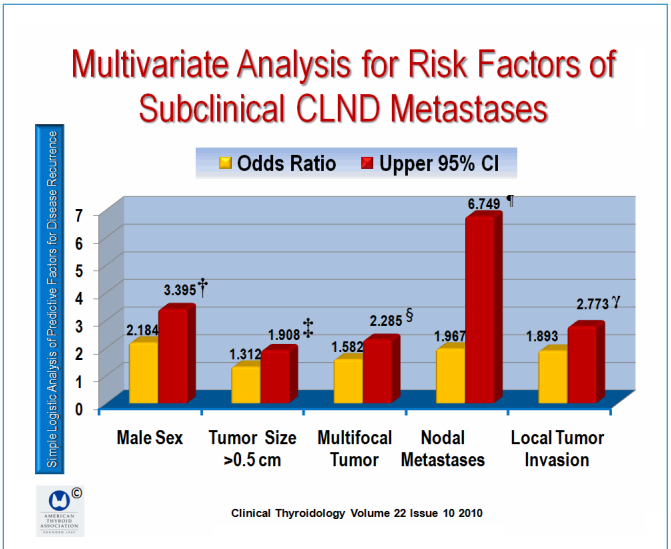

Figure 4. This figure shows the results of multivariate analysis for risk factors of subclinical CLND metastases. The odds ratio and upper 95th percentile are shown. CI = confidence interval; CLND = central-neck lymph-node dissection. †P = 0.001. ‡P = 0.156. §P = 0.015. ¶ P = 0.282. γP = 0.01.

COMMENTARY

The debate concerning routine prophylactic CLND for PTMC centers on studies that report little benefit for this surgery (1-3). Still, these studies report late recurrence with PTMC even with occasional distant metastases. Others recommend prophylactic CLND for patients ≥45 years of age, including the study by So et al. and others (4-8). For example Mercante et al. (9) reported that total thyroidectomy seems advisable in PTMC with extrathyroidal extension and neck lymph-node metastasis at the time of presentation and that capsular invasion without extrathyroidal extension may suggest aggressive tumor behavior and require radical treatment.

There are several studies that found BRAF mutations in patients with PTMC may identify patients with more aggressive tumor behavior, despite the small size of the tumor (10).

Most experts suggest that CLND be performed by high-volume surgeons who are trained for this procedure. Lastly, there is evidence that selected small PTMCs require RRA, which is facilitated by CLND (11).

— Ernest L. Mazzaferri, MD, MACP

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DISCLOSURE

Dr. Mazzaferri is a consultant to Genzyme.

Dr. Sipos Lectures for Abbott Pharmaceutical and Genzyme.

Call for Proposals – American Thyroid Association (ATA) Research Grants
Deadline: January 31, 2011

Electronic Submission: Proposals should be submitted electronically through the research grant application feature on the ATA website, www.thyroid.org.

The American Thyroid Association (ATA) is pleased to announce the availability of funds to support new investigator initiated research projects in the area of thyroid function and disease. Topics may include, but are not limited to, clinical thyroidology, thyroid autoimmunity, thyroid and the brain, thyroid cancer, medullary thyroid cancer, thyroid hormone action and metabolism, and thyroid cell biology. Research awards are intended to assist new investigators in obtaining preliminary data for submission of a more substantial application (i.e., to the NIH). Research grants, up to $25,000 annually, will be awarded for two year terms based on receipt and review of a satisfactory progress report from funded investigators in the fourth quarter of the first year of funding.

Guidelines for All Research Grant Proposals: As mentioned above, research awards are targeted for funding of new investigators to obtain preliminary data for submission of a more substantial application (i.e., to the NIH). Interested investigators should submit a brief description of the proposed research by January 31, 2011.

Eligibility of Applicant and Use of Funds Guidelines:

1. New investigators are individuals who are less than 6 years from completion of their post-doctoral fellowship and have never been a PI on an NIH RO1 or equivalent grant (recipients of NIH R29, R21 and KO8 awards are eligible).
2. Faculty members (MD and PhD) are eligible.
3. Postdoctoral fellows are eligible if their department provides written confirmation that at the time of the award the applicant will have a junior faculty position.
4. Students working towards an MD or a PhD are not eligible.
5. Investigators and individuals who have previously received ATA, ThyCa or THANC awards are not eligible. In general, investigators who have achieved the rank of associate professor or higher are not eligible.
6. Applications are limited to one per individual researcher.
7. The funds can be used for direct costs associated with the proposal, including technician's salary, supplies or equipment but not for PI's salary.
8. Recipients of ATA grants must be ATA members (submit application online if not already a member). For new members, membership dues for the first year will be waived.

Proposal Requirements: The following documents must be submitted online:

1. **Grant Proposal** (A **s**hort proposal that should be no longer than 900 words or three double-spaced pages in 12 point type. These space requirements are absolute and nonconformance will preclude review.)This short proposal should include:
   - Name /affiliation of applicant, complete work/home contact information
   - Title of proposed study
   - Background to the project
   - Hypothesis and/or outline of proposed studies
   - Outline of methodology
   - Anticipated results and implications
   - A short statement of how the grant will aid the applicant
   - References (selected)
2. CV (NIH-style CV – up to 4 pages - including evidence that the applicant is a new investigator with date of completion of postdoctoral training and current grant support (if any). In the case of postdoctoral fellows, written confirmation from the department chair must be provided that the applicant will have a junior faculty position at the time of the award. **Note: Without a suitable CV, applications will not be considered.**
3. Cover letter

Grant Review: The ATA Research Committee will rank proposals according to their scientific merit. Authors of selected proposals will be notified in March 2011 and invited to submit a complete grant application.

American Thyroid Association (ATA)

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

ATA Webinars: Education When and Where You Want It!

As awareness and the prevalence of thyroid disease and its related disorders grows so also arises the need for education of health care professionals and the general public. The American Thyroid Association remains at the forefront of CME certified thyroid education. We invite you to join us for our new series of webinars beginning in the Spring of 2011. CME Credit will be available for each webinar.

Revisit **http://www.thyroid.org/professionals/education/webinars.html**
in the coming months for webinar dates, times and registration information.

Practical Lessons from the ATA Guidelines for the Management of Thyroid Nodules

Speaker: David S. Cooper, MD, Johns Hopkins University

Practical Lessons from the ATA Guidelines for the Management of Differentiated Thyroid Cancer

Speaker: David S. Cooper, MD, Johns Hopkins University

Hypothyroidism LT4-LT3 Therapy

Speaker: Michael T. McDermott, MD, University of Colorado Denver

Target Audience (Who Should Attend): The ATA remains at the forefront of CME accredited thyroid education. ATA webinars are designed for thyroid specialists: endocrinologists, internists, surgeons, basic scientists, nuclear medicine scientists, pathologists, endocrine nurses, physicians 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.

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, or for ordering a recording with your registration.

Learning Objectives: At the conclusion of each webinar, 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 enhance 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 on-screen at the live webinar.

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The American Thyroid Association - *ATA Webinars: Education When and Where You Want It!*
6066 Leesburg Pike, Suite 550, Falls Church, VA 22041 - Questions, please call (703) 998-8890 or email us at thyroid@thyroid.org.
Visit the ATA website at www.thyroid.org for registration details and updates on future webinar and live events.

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