

Preparation of thyroid remnant ablation using recombinant human TSH and 30 mCi of ¹³¹I is as effective as thyroid hormone withdrawal

Lee J, Yun MJ, Nam KH, Chung WY, Soh EY, Park CS. Quality of life and effectiveness comparisons of thyroxine withdrawal, triiodothyronine withdrawal, and recombinant thyroid-stimulating hormone administration for low-dose radioiodine remnant ablation of differentiated thyroid carcinoma. *Thyroid* 2010;20:173-9.

SUMMARY

BACKGROUND

Few studies have examined the efficacy of 30 mCi of radioiodine (¹³¹I) using recombinant human thyrotropin- α (rhTSH) in preparation for thyroid radioiodine remnant ablation (TRRA) with 30 mCi in low-risk patients with differentiated thyroid cancer. This study investigated whether preparation with rhTSH was comparable to conventional preparation with thyroid hormone withdrawal (THW), providing the same therapeutic effect as preparing patients with rhTSH. The study also compared the quality of life (QOL) of patients with thyroid cancer who were prepared with rhTSH versus those prepared with THW.

METHODS

This is a randomized, controlled, open-label, single center study designed to compare the efficacy of various patient preparation methods prior to postsurgical remnant ablation using 30 mCi of radioactive iodine (¹³¹I) and to explore the QOL of patients being treated with ¹³¹I.

Patients age 18 years of age or older who recently were treated for differentiated thyroid cancer (DTC) with total or near-total thyroidectomy and central-compartment neck dissection were recruited for this study from February 2006 through March 2007. Excluded from the study were patients who had evidence of distant metastases (M1), lateral cervical lymph-node

metastases (N1b) with or without significant extrathyroidal tumor invasion (T₄), clinical laboratory studies showing hematologic or blood chemistry abnormalities, or abnormal serum creatinine levels. After surgery, all patients were started on 2 μ g/kg of levothyroxine (L-T₄).

At least 30 days after surgery, patients were randomly assigned to one of three groups: the L-T₄ withdrawal group (T₄-WD) in which L-T₄ was discontinued for 4 weeks; the T₃ (triiodothyronine) withdrawal group (T₃-WD) in which L-T₄ was discontinued for 4 weeks followed by 2 weeks on and 2 weeks off L-4 before ¹³¹I; and the rhTSH group that was on L-T₄ since surgery with a short cessation for 4 days prior to the day of rhTSH administration.

All patients were on a 2-week low-iodine diet prior to ¹³¹I therapy, and all had a 24-hour urine test and creatinine excretion measurement on the final day of the low-iodine diet. The authors devised a seven-item written QOL questionnaire to measure the impact of social life and mood changes and medical resource utilization. The success of TRRA was assessed at 12 months with a whole-body diagnostic ¹³¹I scan (DXWBS), serum thyroglobulin (Tg) measurement after TSH stimulation, and neck ultrasonography.

RESULTS

Patient Characteristics (Figures 1 and 2)

A total of 291 patients were recruited into the study and randomly assigned into the three study groups after total thyroidectomy.

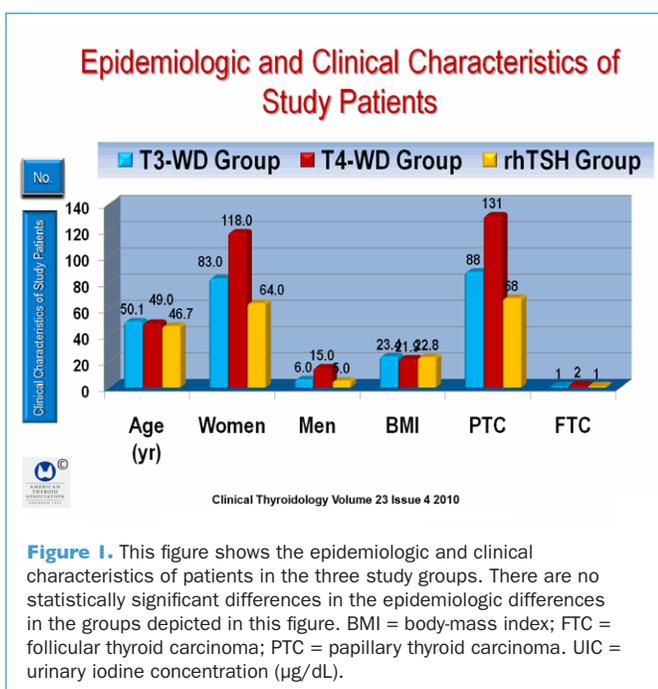


Figure 1. This figure shows the epidemiologic and clinical characteristics of patients in the three study groups. There are no statistically significant differences in the epidemiologic differences in the groups depicted in this figure. BMI = body-mass index; FTC = follicular thyroid carcinoma; PTC = papillary thyroid carcinoma. UIC = urinary iodine concentration (μ g/dL).

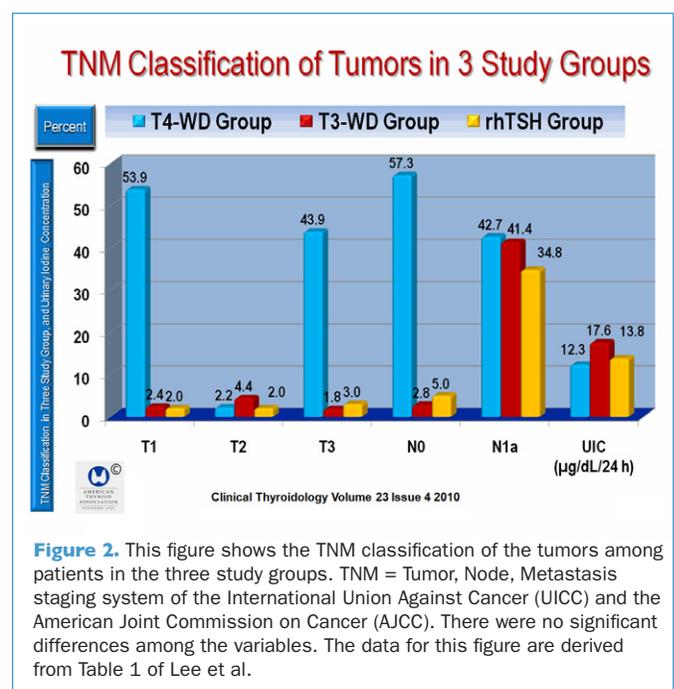


Figure 2. This figure shows the TNM classification of the tumors among patients in the three study groups. TNM = Tumor, Node, Metastasis staging system of the International Union Against Cancer (UICC) and the American Joint Commission on Cancer (AJCC). There were no significant differences among the variables. The data for this figure are derived from Table 1 of Lee et al.

Patient demographics and tumor stage are shown in Figure 1. There was no significant difference in age, ratio of women to men, body-mass index, and ratio of papillary to follicular cancer among the three groups. After 12 months of follow-up, the mean (\pm SD) serum Tg levels after TSH stimulation were 0.18 ± 0.14 ng/ml (range, 0.01 to 2.9) in the T₄-WD group, 0.14 ± 1.9 (range, 0.1 to 2.9) in the T₃-WD group, and 0.14 ± 0.05 ng/ml (range, 0.1 to 0.2) in the rhTSH group. There were no statistically significant differences in the tumor–node–metastasis (TNM) tumor classifications in the three groups (Figure 2).

TRRA Outcomes among the Three Study Groups (Figure 3)

To assess the efficacy of each preparation method, each patient had a DXWBS, neck ultrasonography, and TSH-stimulated serum Tg measurement at 12 months. The comparative ablation rates are shown in Figure 3. The rhTSH ablation rate was equivalent to that achieved by the two THW groups. In the T₄-WD group, serum Tg >1.0 ng/ml (n = 8) was associated with persistent residual thyroid tissue in six patients and with two lymph-node metastases identified by DXWBS and neck ultrasonography.

In the T₃-WD group, 10 patients had elevated serum Tg levels associated with persistent residual disease in seven patients with lymph-node metastases that were detected by neck ultrasonography in three patients but were missed by DXWBS

in one patient. In the rhTSH group, detectable serum Tg was found in five patients, which was associated with a persistent thyroid remnant in three, with lymph-node metastases detected by DXWBS in two patients, but was missed by ultrasonography. Five patients, (two in T₄-WD group, two in the T₃-WD, and one in the rhTSH group, had lymph-node metastases that persisted after surgery and disappeared after the second ¹³¹I ablation and was verified by DXWBS, neck ultrasonography, and undetectable serum Tg, and in 2 patients (one in the T₃-WD group and one in the rhTSH group) missed by DXWBS but identified by TSH-stimulated serum Tg and neck ultrasonography was confirmed by fine-needle aspiration biopsy.

Quality of Life (Figure 4)

There was a highly significant difference in QOL status between the three thyroid hormone withdrawal groups (T₄-WD and T₃-WD groups), and the rhTSH group. Still, there was no difference in the QOL during preparation for DXWBS between patients in the two thyroid hormone withdrawal groups (Figure 4).

CONCLUSION

The use of rhTSH effectively stimulated the uptake of 30 mCi of ¹³¹I for thyroid remnant ablation as effectively as thyroid hormone withdrawal and maintains the QOL of patients who are remaining euthyroid during preparation for thyroid remnant ablation.

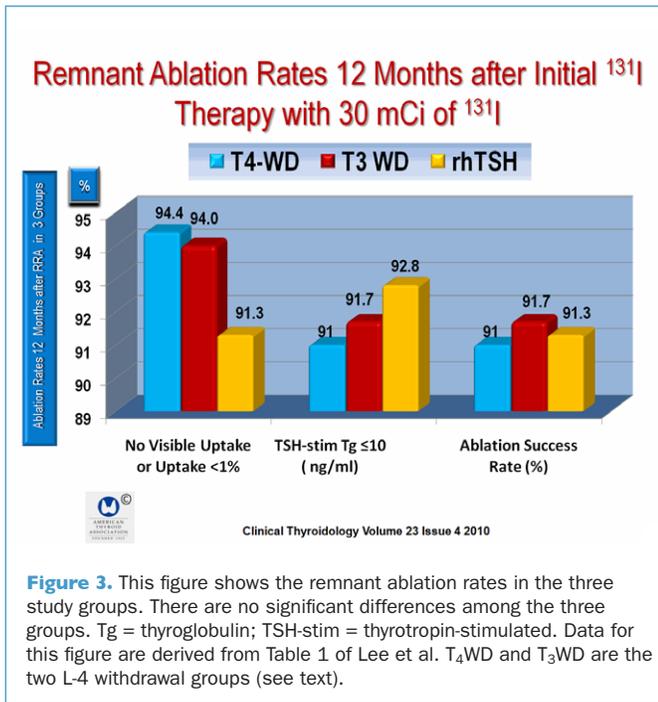


Figure 3. This figure shows the remnant ablation rates in the three study groups. There are no significant differences among the three groups. Tg = thyroglobulin; TSH-stim = thyrotropin-stimulated. Data for this figure are derived from Table 1 of Lee et al. T₄WD and T₃WD are the two L-4 withdrawal groups (see text).

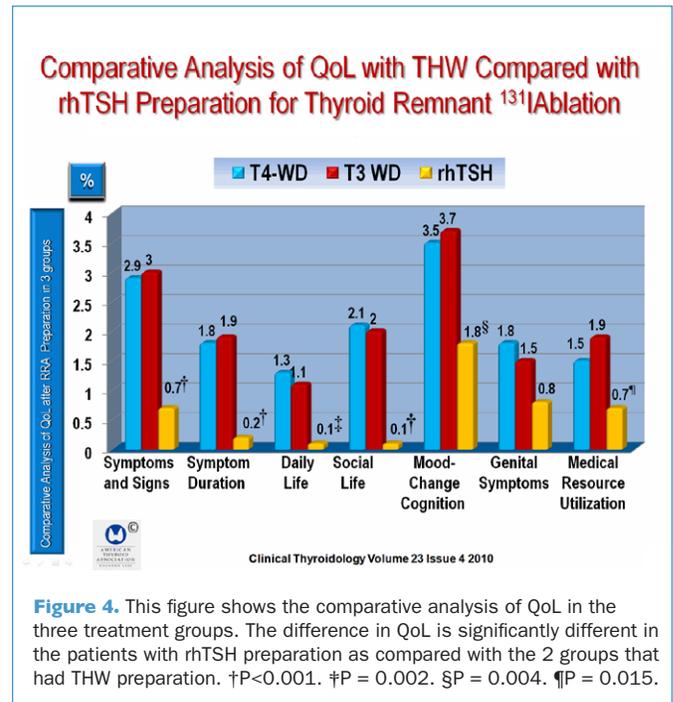


Figure 4. This figure shows the comparative analysis of QoL in the three treatment groups. The difference in QoL is significantly different in the patients with rhTSH preparation as compared with the 2 groups that had THW preparation. †P < 0.001. ‡P = 0.002. §P = 0.004. ¶P = 0.015.

COMMENTARY

This is one of the few prospective, randomized studies that analyze the efficacy of 30 mCi of ^{131}I for TRRA (1), and even fewer compare rhTSH-stimulated TRRA with 30 mCi as compared with THW (2). The main message from the Lee study is that rhTSH is at least as effective as THW in preparation for TRRA with 30 mCi (2). In fact, after 12 months of follow-up, the mean success TRRA rate was over 90% in all three study groups. This is a bit higher than usual, which may be the result of several factors. The results were reported after a 12-month follow-up during which patients were deemed to have successful TRRA based on no visible ^{131}I neck uptake or an uptake $<1\%$ and a negative DXWBS and neck ultrasonography and a TSH-stimulated $\text{Tg} \leq 10$ ng/ml. While this may be a reasonable end point to identify patients who have no evidence of disease, one would be more certain about the completeness of TRRA with a TSH-stimulated Tg that is undetectable (3). Still, the rhTSH-stimulated Tg was

in the same range as those of patients in the two THW groups. Another reason for the high TRRA success rate may be because all patients had good adherence to a low-iodine diet. Although some have suggested that there is enough iodine in L-4 to blunt the therapeutic effect of ^{131}I in patients treated with rhTSH (2), prospective studies have failed to confirm this finding (4). In the Lee study, the rhTSH group had a 4-day L-4 withdrawal just before rhTSH was administered, and it is not likely that this had a robust effect on TRRA.

The most important finding in this carefully crafted study is that rhTSH can be used in lieu of thyroid hormone withdrawal, and patients with low-risk thyroid cancer can be prepared for TRRA using rhTSH with very small amounts of ^{131}I , in the range of 30 mCi, thus diminishing total-body irradiation and decreasing damage to nonthyroidal tissues.

— Ernest L. Mazzaferri, MD, MACP

References

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