Journal of
Endocrinology and Thyroid Research
ISSN: 2573-2188

Juniper Publishers
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Mini Review
Volume 1 Issue 2 - March 2017
DOI: 10.19080/JETR.2017.01.555558

J Endocrinol Thyroid Res

Use of Personalized Post-Total Thyroidectomy Criteria in Low and Intermediate Risk Papillary Thyroid Cancer Patients to avoid Routine Radioactive Iodine Administration

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Submission: February 12, 2017; **Published:** March 17, 2017

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Mini Review

In the treatment of many types of cancer, clinicians are required to make assessments of patient risk based on a range of factors and then tailor treatment to reflect that level of risk. A recent study from our centre has shown that the use of several personalized criteria in low and intermediate-risk papillary thyroid cancer (PTC) patients after treatment by a total thyroidectomy can avoid routine radioactive iodine remnant ablation (RAI) in the vast majority of such patients.

The Administration of RAI to PTC Patients

Each year an estimated 62,000 people in the US are diagnosed with thyroid cancer [1], a significant percentage of patients undergo total thyroidectomy for a total removal of the thyroid gland and any gross central compartment lymph nodes when indicated. This treatment option has proved to be highly effective for managing most PTC patients when combined with long term serum TSH suppression using thyroxine administration.

To eliminate remaining potential residual normal and or cancer thyroid cells, many PTC patients have been routinely receiving RAI at varying dosages. The American Thyroid Association (ATA) guidelines state that use of remnant ablation involving administration of RAI may be appropriate for many PTC patients, including some low-risk patients [2]. In recent years, there have also been some uncertainly about the benefits of RAI remnant ablation to reduce the risk of recurrence, especially among patients with low-risk papillary thyroid cancer (PTC). We and others have demonstrated that many total thyroidectomy PTC patients can be shown to often have achieved a TSH-stimulated thyroglobulin (Stim-Tg) levels less than 1µg/L before RAI, making the risk for recurrence or death very unlikely [3-7]. Such PTC patients can be safely followed using combined neck ultrasound and serum thyroglobulin levels as a reliable indicator of residual or recurrent PTC when there is no detectable anti thyroglobulin antibody to interfere with the accurate measurement of thyroglobulin. In addition, literature reports have not demonstrated that RAI therapy decreases recurrence rates or risk of death in low-risk PTC patients [8-10].

While ATA guidelines support "selective use" of RAI for low- and intermediate-risk PTC patients, objective criteria to support its use are generally not available [2,11,12]. Lack of clear guidelines and conflicting opinions among clinicians in recent years [13,14] have supported the routine administration of RAI. In light of the lack of data demonstrating a clear benefit from RAI and the potential [16-19] health risks associated with RAI, our center [15] and others have worked to develop a more effective strategy to determine which low and intermediate - risk PTC patients should be treated with RAI [4]. Such personalized criteria are based upon post-operative pathology findings, Stim-Tg and neck ultrasound for each PTC patient in our cohort. Using this protocol, we have demonstrated that this approach can assist in determining which PTC patients may safely avoid routine RAI and select those that may benefit from such therapy.

Research Findings

In our long term prospective research report follow up data at a mean duration of 6.2 years was obtained from low and intermediate-risk PTC patients who previously were treated with a total thyroidectomy [3,4,15]. Low-and intermediate-risk was defined as all PTC nodules equal or greater than 1cm (T1-T3),

confined to the thyroid or central (level VI) lymphnodes (N0-N1a), irrespective of patient age or tumor size. Exclusion criteria included (1) tumors less than 1cm given that their risk for PTC recurrence was defined as very low, (2) detectable anti-thyroglobulin antibodies (TgAb) given their potential interference with the thyroglobulin (Tg) assay, (3) lateral compartment lymph node involvement (N1b) and (4) extra-thyroidal extension (T4) or distant metastases (M1). The study also collected relevant demographic, surgical, pathologic, lab biochemistry, treatment and clinical outcome data [15].

All patients underwent a post-operative stimulated thyroglobulin (Stim-Tg) and neck ultrasound approximately three months after their thyroidectomy [15]. The sub-group of patients with Stim-Tg measurements less than 1μg/L was informed that the thyroidectomy was likely curative and that there was no definite indication for administration of RAI. Patients with Stim-Tg greater than 1μg/L but less than 5μg/L were informed that there was no immediate indication for RAI and could be followed by active surveillance to validate the absence of a risk for residual thyroid cancer by no significant changes in the follow up Stim-Tg and neck ultrasound. However, patients with a Stim-Tg greater than 5μg/L were strongly advised to proceed with RAI therapy [15].

All patients were followed on long-term thyroid hormone TSH-suppression therapy with repeat neck ultrasound and Stim-Tg measurements every 6-12 months. Patients who received RAI had a whole-body scan (WBS) seven days after treatment. A total of 129 low/intermediate-risk PTC patients were followed prospectively for a mean duration of 6.2 years.

Conclusion

Among the 129 PTC patients who were stratified as low/intermediate-risk, 116 (90%) were able to avoid RAI using this strategy with a mean prospective follow-up of 6.2 years and virtually no risk of residual/recurrent disease. (A single patient who had evidence of residual/recurrent disease was correctly identified to receive RAI using this strategy). The overall risk for residual/recurrent PTC was less than 1%, and no patients required RAI at a subsequent two-year follow up to a mean of 8.2 years.

These findings from our center published by Orlov et al. [15] provide the first long-term prospective study cohort with a mean follow up of over eight years and support use of serial post-operative stimulated thyroglobulin and neck ultrasound as personalized criteria for risk stratification. They further support the use of this strategy for RAI administration in low- and intermediate-risk papillary thyroid cancer. In this innovative prospective study, the vast majority of low/intermediate-risk PTC patients were able to avoid RAI. These observations demonstrate that risk factors derived from PTC age and lesion size and previously considered to favor RAI treatment are not in accord with the objective prospective personalized strategy criteria that we have developed for the improved identification of those PTC patients who can safely avoid RAI. Consequently, this personalized strategy will vary significantly lower the incidence of RAI administration in the vast majority of low and intermediate-risk PTC cohorts after a total thyroidectomy and will also reduce in health care costs, patient inconvenience, and potential radiation exposure side effects.

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How to cite this article: Paul G W.Use of Personalized Post-Total Thyroidectomy Criteria in Low and Intermediate Risk Papillary Thyroid Cancer Patients to avoid Routine Radioactive Iodine Administration. J Endocrinol Thyroid Res. 2017; 1(2): 555558. DOI: 10.19080/JETR.2017.01.555558

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