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Delaying Radioactive Iodine Ablation for up to One Year Does Not Increase Recurrence for Patients with Differentiated Thyroid Cancer

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SUMMARY

Background

Patients with differentiated thyroid cancer (DTC) who undergo total thyroidectomy are candidates for adjuvant radioactive iodine ablation (RAI). RAI is used to treat presumed or known residual local disease or distant metastases, with a secondary objective of ablating the normal thyroid remnant to facilitate post-operative surveillance using thyroglobulin levels. The 2015 American Thyroid Association (ATA) guidelines recommend selective use of RAI for intermediate- and high-risk tumors, and using low-dose RAI or omitting it for most low-risk tumors (1). The optimal timing of RAI following thyroidectomy has been debated, and it is largely determined by logistics that include patient convenience and need for hospitalization. The current study evaluated the impact of the time interval between thyroidectomy and RAI administration on disease outcomes.

Methods

This was a retrospective analysis of consecutive patients with DTC who were treated at a tertiary referral center in Brazil from 2000 through 2015. Patients with DTC were included if they underwent total thyroidectomy with or without lymph-node dissection followed by RAI ablation and suppression with levothyroxine. All patients were prepared for RAI with levothyroxine withdrawal, confirmed by a TSH >30 mIU/L at the time of RAI administration. The interval between surgery and RAI was determined by patients' access to limited local medical facilities, as doses of RAI >49.9 mCi require inpatient hospitalization in Brazil.

Patients were separated into two groups by time between surgery and RAI ablation: group A ≤6 months and group B >6 months. Follow-up surveillance included thyroglobulin levels and cervical ultrasound. The main outcome was disease-free status as defined by the absence of biochemical or structural disease at 1 year and 6 years after thyroidectomy. Thyroglobulin levels of <1 ng/ml (suppressed) and <2 ng/ml (stimulated) were used as cutoffs for biochemical disease-free status. Recurrence was defined by new biochemical or structural disease in a patient who was previously considered free of disease.

Results

Of 901 patients with DTC, 545 underwent total thyroidectomy followed by RAI ablation. An additional 180 patients had thyroidectomy but were not treated with RAI, and 176 were lost to follow-up and were excluded from the analysis. The rate of RAI use for patients with DTC who underwent surgery during the study period was 80%. The median tumor size of the study cohort was 2.0 cm. One third had cervical-lymph-node metastases, and 9.2% of patients had distant metastases. The ATA risk stratification was low in 41.8% of patients, intermediate in 45.0% of patients, and high in 13.2% of patients. The mean (±SD) RAI dose was 112.3±38.1 mCi.

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For the entire cohort, the median time from surgery to RAI was 6 months (interquartile range [IQR], 3–10). Group A (295 patients) had a median interval of 3 months (IQR, 2–5) and group B (250 patients) had a median interval of 10.5 months (IQR, 8–16). Patients in group B were slightly older (47.1 years vs. 43.1 years, P<0.01), less likely to have nodal metastases (26.4% vs. 40.7%, P<0.01), and more likely to be ATA low-risk (48.0% vs. 36.6%, P = 0.027) as compared with group A.

At 1 year after initial thyroidectomy, no significant difference in disease-free status was observed (59.3% for group A vs. 65.6% for group B, P = 0.15). At a median follow-up of 6 years, the rate of disease-free status remained similar between groups A and B (63.3% vs. 67.7%, P = 0.31). The recurrence rates in the two groups were also similar (5.4% vs. 3.0%, P = 0.39). This trend was seen across all ATA risk categories. In multivariable analysis, the time between thyroidectomy and RAI ablation was not a significant predictor of disease status.

Conclusions

The time between thyroidectomy and RAI ablation does not impact disease outcomes in patients with DTC, regardless of initial extent of disease. RAI ablation can be scheduled within 1 year after surgery according to patient convenience and availability of health care resources.

ANALYSIS AND COMMENTARY

Routine RAI ablation is no longer recommended after thyroidectomy for all patients with DTC. Data to support decreased local recurrence and improved survival following RAI is largely limited to high-risk tumors (gross extrathyroidal extension or distant metastases) (2, 3). Given the less clear benefit for low- and even intermediate-risk patients, flexibility in timing is ideal to optimize patient convenience and health care utilization. The current study suggests that delaying RAI for up to 1 year after surgery does not compromise disease outcomes.

Few prior studies have examined the impact of the interval between surgery and RAI. In a study from Japan of 198 patients with high-risk DTC, an interval between thyroidectomy and RAI of >6 months was associated with a fourfold higher disease-specific mortality (4). However, that study included only patients with advanced disease (distant metastases or gross extrathyroidal extension). In addition, the mean interval between surgery and RAI was 2.6 years, mainly because of delayed surgeon referral or limited resources for inpatient hospitalization to administer RAI. Another study from Greece of 107 patients with low-risk DTC showed no difference in disease outcomes between patients who underwent RAI ablation at a median of 3 months versus 6 months after thyroidectomy (5).

The current study is a retrospective analysis conducted at a single institution over a 15-year period. The rate of RAI administration was very high, likely reflecting older practice guidelines that recommended more routine use of RAI even for patients with low-risk DTC. It is likely that the use of RAI decreased over the study period, although this is not mentioned in the article. This is an important potential confounder that should have been accounted for in the study. In addition, patients in group B may have had delayed RAI because they were considered to be at lower risk by their physicians or had less access to medical care. Although the authors performed a multivariable analysis that accounted for disease burden, it remains difficult to isolate the impact of time between surgery and RAI in a retrospective study. The authors did perform a subgroup analysis by ATA risk category, an important predictor of persistent and recurrent disease that accounts for the initial extent of disease.

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This study as well as the study from Japan highlights potential limitations in health care resources, especially when RAI must be administered in an inpatient hospital setting because of patient logistics or local legislation. Considering all the available data, delaying RAI for up to 1 year after thyroidectomy likely has no impact on disease outcomes, especially for low- and intermediate-risk patients. Patients should be counseled accordingly, allowing them to schedule RAI to minimize interference with major life events. Most patients with low-risk DTC who have an excellent response to initial surgical treatment will not benefit from RAI ablation, which may free up resources for higher-risk patients. Consideration should also be given for lower doses of RAI, such as 30 mCi, which can more readily be administered without hospitalization.

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