WITH THE RISING INCIDENCE OF SECOND CANCERS, SHOULD YOU GIVE RAI TO A LOW-RISK (T1N0) THYROID CANCER PATIENT?

Iyher NG, Morris LG, Tuttle RM, Shaha AR, Ganly I. **Rising incidence of second cancers in patients with low-risk (T1N0) thyroid cancer who receive radioactive iodine therapy.** Cancer. March 22, 2011 [Epub ahead of print]. doi: 10.1002/cncr.26070.

SUMMARY

BACKGROUND

An increase in secondary primary malignancies (SPM) after radioactive iodine (RAI) therapy for differentiated thyroid is a risk that has been seriously recognized for the past 8 years, since the initial report by Rubino et al. (1). During this time, several papers (2) explored this question using the Surveillance, Epidemiology, and End Results (SEER) database of the National Cancer Institute, but the purpose of this reanalysis is to determine specifically the pattern in the increase in use of RAI and the pattern of increase of SPM in low-risk patients with differentiated thyroid cancer.

METHODS

The SEER 13 cohort database (1973–2006) was queried for patients diagnosed with well-differentiated thyroid cancer (WDTC) including papillary, follicular variant of papillary, and follicular thyroid carcinoma. Patients were excluded if any of the following data were missing: tumor size, extrathyroidal extension, lymph-node status, metastasis status, or RAI administration. Low-risk tumors were defined as those <2 cm intrathyroidal tumors without extrathyroidal extension, lymph-node metastases, or distant metastases in patients <45 years of age. An SPM was defined as a solid or hematologic malignancy that occurs >6 months after diagnosis. The risk of SPM is the standardized incidence ratio (SIR)—the ratio of observed to expected (O/E) second cancers. The excess absolute risk represents the absolute number of additional second cancers attributable to RAI treatment and is calculated as the excess (O/E) number of second cancers in patients per 10,000 person-years at risk.

RESULTS

WDTC has increased in incidence from 3.5 per 100,000 population in 1973 to 11.4 per 100,000 in 2007. Thyroid tumor size has been recorded since 1983. Since 1983, the incidence of low-risk WDTC has increased from 1.2 to 5.2 per 100,000, which accounts for the majority (55.6%) of the increased incidence of WDTC. Among patients <45 years of age who have low-risk tumors, RAI treatment increased from 3.3% in 1973 to 38.1% in 2006. As expected, the rate of overall survival among patients with low-risk WDTC has remained constant during this period, at nearly 100%. For all patients with WDTC, the SIR of SPM at any site was 1.18 (95% confidence interval [CI], 1.10 to 1.25). The SPMs with significantly elevated risk because of RAI were cancers of the salivary gland (SIR, 3.84; 95% CI, 1.66 to 7.56) and kidneys (SIR, 2.62; 95% CI, 1.94 to 3.47) and leukemia (SIR, 2.09; 95% CI, 1.49 to 2.86). The risk of leukemia was especially high in patient <45 year of age (SIR, 5.32; 95% CI, 2.75 to 9.30) as compared with older patients (SIR, 2.26; 95% CI, 1.43 to 3.39).

CONCLUSIONS

In the past three decades, the incidence of thyroid cancer has increased more than threefold. Many groups have argued that this increase is due to incidental detection from the increased use of head and neck imaging studies, but nearly 50% of the increased incidence is from tumors >2 cm, suggesting that a significant number of patients have clinically important tumors. The proportion of tumors that were considered low risk in 2007 was 45.6%. Despite the increase in proportion of low-risk tumors, the use of RAI for WDTC has remarkably increased, according to this report to nearly 40% in the low-risk category. Although the rates of RAI increased, overall survival remains excellent, at nearly 100%. This report demonstrates that there were no excess SPMs during the time that RAI was less commonly used in 1973–1981, and the rise in SPM was stepwise over the time that the use of RAI was increasing. The fact that the shapes of the curves of the rise in SPM and the use of RAI are not similar suggests that there may be other factors involved in the development of SPM.

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COMMENTARY

We are faced with increasing numbers of new cases of thyroid cancer (3) and need to make a decision about treatment. Consideration for RAI ablation must include not only the increase in risk of chronic complications including sialadenitis, dry mouth, and tooth loss, but also the increased risk of SPM in low-risk patients. This is especially worrisome with the increased risk of leukemia in patients <45 years old, as compared with older patients. Since the mid-1980s when I did my fellowship, we practiced in a way to destroy every molecule of thyroid cancer, and nearly every patient I saw received an ablation dose of RAI. I now have changed my practice because of the evidence of SPM after RAI. In 2011, I think we must consider not using RAI ablation in our patients with low-risk thyroid cancer and realize that the complications do not justify the ability to use a post-therapy thyroglobulin as a tumor marker or an RAI whole-body scan to detect tumor recurrence. No studies, including this one, have shown a significant reduction in the already low mortality in patients with low-risk (<2 cm intrathyroidal) WDTC with RAI ablation. I am actively changing my practice as I have more carefully reviewed the literature and do not give RAI ablation to patients with small tumors (<1.5 cm) without extrathyroidal or capsule invasion, positive nodes, or distant disease. Further, when I do treat, I am reducing the whole-body radiation exposure by decreasing the dose of RAI and administering remnant ablation after recombinant human TSH stimulation. I have not yet jumped to not using RAI therapy in primary tumors >2 cm, but I will consider that as additional data are published.

— Stephanie L. Lee, MD, PhD

References

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