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Recurrence of Papillary Thyroid Cancer Was Found in 1.4% of Those Without Persistent Disease Within 8 Years

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Durante C, Montesano T, Torlontano M, Attard M, Monzani F, Tumino S, Costante G, Meringolo D, Bruno R, Trulli F, Massa M, Maniglia A, D'Apollo R, Giacomelli L, Ronga G, Filetti S; on behalf of the PTC Study Group. Papillary thyroid cancer: time course of recurrences during postsurgery surveillance. J Clin Endocrinol Metab 2013;98:636-42. Epub January 4, 2013.

SUMMARY

Background

Because some patients with papillary thyroid cancer (PTC) have late recurrences, these patients are followed for many years. Currently, most patients with PTC have small tumors and a very good prognosis. The tools for following these patients have improved in the past two decades, so recurrences are detected more easily. The question of how long and how frequently patients with PTC should be followed has not been addressed. The present study was conducted to identify times to recurrence of PTC and to define the rates of recurrences in order to provide data to improve the cost-effectiveness of postoperative surveillance.

Methods

This is a retrospective study of consecutive patients with PTC diagnosed since January 1990 in eight Italian referral centers. Inclusion criteria were negative antithyroglobulin levels and follow-up for at least 3 years before January 31, 2012. All patients had total thyroidectomy. The use of cervical-lymph-node dissection and radioiodine ablation (RAI) was based on institutional guidelines. Patients had follow-up within the first year and then yearly thereafter that included neck ultrasound and serum Tg, basal and stimulated. Suspicious lymph nodes were biopsied, and appropriate imaging studies were performed to identify structural disease.

Results

The study population consisted of 1020 patients, 80% of whom were female. The median tumor size was 15 mm; tumors were multifocal in 36% and bi-lateral in 25%. Extrathyroidal extension was found in 245 patients, positive lymph nodes in 255, and distant metastases in 3.2%; 82% were classified as AJCC stages I or II. The ATA risk level (1) based on the surgical findings and pathology was low in 61.3%, intermediate in 35.5%, and high in 3.2%. Radioiodine remnant ablation was performed in 88% of the patients.

In the first postoperative follow-up, persistent disease was found in 72 (7.2%), and 57 of them had positive serum Tg. Those with persistent disease comprised 16 (2.5%) of the 625 with low risk, 41 (11.3%) of the 362 with intermediate risk, and 23 (69.7%) of the 33 with high risk. At the end of the follow-up (5 to 20 years; median, 10 years), 20% of the group still had imaging-documented disease and 80% were disease-free. Imaging was negative and Tg positive in 18.5% who received RAI and in 15.2% of those who did not.

Of the 948 patients considered to be disease-free based on initial postoperative imaging, 185 (15%) had positive Tg. Disease recurred in only 1 of the 185 patients with detectable Tg and no structural disease. It recurred in 13 of the 948 (1.4%) within 8 years, half of them within the first 3 years; 5 were low-risk and 8 intermediate-risk patients. Only 6 of the 13 had positive Tg at recurrence.

Conclusions

Recurrence of PTC is uncommon but may occur within 8 years of follow-up in 1.3% of patients at intermediate and low risk.

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ANALYSIS AND COMMENTARY

This paper provides important data regarding long-term follow-up of patients with PTC, but it does not provide a definitive rationale for optimal management of these patients with regard to length of follow-up before saying that recurrent disease is very unlikely. Persistent disease in 2.5% and recurrence in 0.8% (5 of 625) of the low-risk group are cause for concern. The authors contrast their findings with the 1990 findings of Mazzaferri and Jhiang, who found a recurrence rate of 20%, with 19% detected more than 10 years after surgery (2).

Obviously, high-risk patients require long-term, perhaps 20 years, of careful follow-up. Those with low and intermediate risk should probably be followed for 10 years (at least 8, based on the data of this study) before being optimistic about cure, a term used very cautiously, even in patients with thyroid cancer.

Surprisingly, the authors do not comment on what happened to the185 patients with positive Tg at the initial (probably 1 year) follow-up. These patients are certainly a cause for concern and continued follow-up until the Tg declines and/or all imaging is repeatedly negative.

It is interesting that 88% received RAI. With less use of RAI in low-risk patients with PTC, as currently advocated, there may be more cause for concern. The serum Tg in patients who do not undergo ablation will then be detectable often, making this measurement useless as a biomarker for recurrence. The authors point out that 92% of those treated with RAI had negative imaging findings, as did 98% of those not given RAI; the small difference may be attributed to not using RAI in patients with a very good prognosis.

The role of TSH suppression with levothyroxine was not addressed in this report. Because of late recurrences, I am reluctant to allow the TSH to be in the normal range until there is good evidence of absence of disease.

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