

# Clinical THYROIDOLOGY

VOLUME 24 • ISSUE 5

MAY 2012

# Radioiodine Ablation Does Not Increase Survival in Patients with Low-Risk Differentiated Thyroid Cancer

Schvartz C, Bonnetain F, Dabakuyo S, Gauthier M, Cueff A, Fieffé S, Pochart JM, Cochet I, Crevisy E, Dalac A, Papathanassiou D, Toubeau. Impact on overall survival of radioactive iodine in low-risk differentiated thyroid cancer patients. J Clin Endocrinol Metab. February 16, 2012 [Epub ahead of print].

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# Background

In recent years, the clinical efficacy of <sup>131</sup>I ablation of possible remnants after surgery for low-risk differentiated thyroid cancer (DTC) has been questioned. Radioiodine ablation (RAI) is not recommended now for low-risk patients with papillary cancers smaller than 1 cm confined to the thyroid. The current paper reports an analysis of recurrence and survival of patients with differentiated cancers up to 4 cm with no other risk factors who had RAI, as compared with a group who did not undergo RAI.

# Methods

The study included 1298 low-risk patients from two French centers, Reims and Dijon, who were treated between 1975 and 2005. The low-risk patients who were included had complete tumor resection, single tumors 1 to 4 cm with negative lymph nodes or without lymph-node dissection (Nx) corresponding to stage 1 for patients under 45 years old and stages 1 and 2 for patients over 45 years old by the TNM classification. They excluded patients with tumors smaller than 1 cm and those with positive lymph nodes or known metastatic disease. Patients were treated by thyroidectomy or lobectomy. In Dijon, all patients received RAI and had a post-therapy scan, whereas in Reims, patients received RAI based on risk factors (age >45, tumor >3 cm). Eighty-eight percent of the patients received 100 mCi and 12% received only 20 mCi. Patients were followed by conventional means, including clinical examination, serum thyroglobulin (Tg), anti-Tg, and neck ultrasound. Overall survival (OS) was defined as the time from diagnosis to death, and disease-free survival (DFS) was defined as the time from diagnosis to recurrence, second cancer, or all-cause death. A high Tg or anti-Tg was not considered as relapse without evidence of recurrent disease. Univariate and multivariate analyses were carried out, and based on the multivariate analysis, the likelihood of having been given RAI, a "propensity score," was determined for each patient. continued on next page

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# Results

The mean age was 47 and 83% of the 1298 patients in the cohort were female; 72% had papillary cancer and 28% had follicular cancer. Thyroidectomy was performed in 81% and lymph-node dissection in 55%. Seventy percent received RAI and 30% did not. The mean follow-up was 10.3 years. Both disease-free and overall survival were slightly but significantly higher in those who were not given RAI. The10-year DFS rates were 88.7% (95% CI, 85.96 to 90.97) for patients treated with RAI and 93.1% (95% CI, 89.68 to 95.47) for patients not treated with RAI (P<0.0013). Recurrences were found in 1.6% of those who received RAI and 1.0% of those who did not receive RAI. Survival did not differ between those who received 100 mCi or 20 mCi RAI. In the multivariate Cox analysis, age and sex were the only two independent prognostic factors associated with DFS and OS. Survival was worse in those over age 45 and in men. The clinical characteristics significantly associated with RAI treatment were age greater than 45 years, male sex, diagnosis before 1998, total thyroidectomy, lymph-node dissection, papillary histology, and pT2 (tumors 2 to 4 cm). Survival curves based on propensity score (i.e., adjusting for factors that predisposed to the use of RAI) did not differ between the RAI and no RAI groups.

# Conclusions

The study failed to prove any survival benefit of RAI after surgery in a large cohort of patients with low-risk DTC.

# ANALYSIS AND COMMENTARY • • • • • •

Like all retrospective studies of this type, regional factors and current modes of practice probably entered into the decisions for RAI ablation therapy. In Dijon, the use of RAI was based on clinical factors such as age, size of the tumor, and perhaps other factors such as sex and whether it was papillary or follicular. Despite the authors sophisticated statistical calculation indicating that the propensity score for using RAI showed that there was no difference in these factors between those who received RAI and those who did not, I suspect that when low-dose RAI was chosen there were considerations, such as an apparently good prognosis and rules requiring hospitalization, that influenced the decision about whether to choose 100 mCi or 20 mCi. The only way to settle the efficacy or lack of benefit of RAI ablation would be a randomized, controlled study that could now perhaps be extended to T2 tumors and possibly follicular carcinomas. However, the authors offer a caveat of possible misclassification of follicular variants of papillary thyroid cancer being diagnosed as follicular cancers in that bygone era. Since true follicular

cancers have a worse prognosis than papillary carcinomas, unless they are minimally invasive into the capsule and show no vascular invasion, many endocrinologists would currently recommend RAI ablation for follicular cancers.

Nevertheless, this study supports the skepticism regarding RAI for low-risk papillary cancers with negative nodes reported from the Mayo Clinic (1). In a review, Sawka et al. concluded that the benefit of RAI in low risk patients with DTC was unclear (2). In a review of the Surveillance, Epidemiology, and End Results American database, Podnos et al. did not find any significant effect of RAI in overall survival with papillary thyroid carcinoma (3). Lastly, Sacks et al., in an extensive recent review of the literature, reported that the majority of studies did not find a statistically significant improvement in mortality or disease-specific survival in patients with low-risk DTC treated with RAI, but improved survival was confirmed for high-risk patients (4).

— Jerome M. Hershman, MD continued on next page

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