Radioactive Iodine Activities for Postsurgical Thyroid Ablation: The Lower the Better

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The initial treatment of differentiated thyroid cancer consists of total or near-total thyroidectomy. Surgery is usually followed by the administration of radioactive iodine activities (RAI) aimed to ablate any remnant thyroid tissue and potential microscopic residual tumor. It is still controversial whether this procedure may have an influence on the mortality rate, but in most series it seems to reduce the risk of regional recurrence and facilitates long-term surveillance based on serum thyroglobulin (Tg) measurement and diagnostic radioiodine whole body scan (WBS). According to several guidelines [1, 2] the recommendations for remnant thyroid ablation are modulated on the basis of risk factors. RAI ablation is indicated in high-risk patients (those with documented, or strongly suspected, residual disease), whereas it is not indicated in very low-risk patients (those with unifocal microcarcinomas, no metastases, and favorable histology). In patients at intermediate risk (those in between the low and high risk), remnant ablation may be indicated but the decision must be individualized.

Effective thyroid ablation requires adequate stimulation by TSH. This may be achieved by thyroid hormone withdrawal (THW) or after recombinant human TSH (rhTSH) administration. The last procedure is considered the method of choice based on several reports [3–5] demonstrating equal efficacy of rhTSH compared to THW. rhTSH-assisted RAI ablative therapy is associated with similar rates of persistent disease and clinical recurrences than those observed after traditional THW preparation, at least in the short-term follow-up [6, 7]. In addition, preparation with either rhTSH or THW appears to have similar adjuvant effects on small-volume RAI-avid disease identified outside the thyroid bed at the time of initial RAI ablation [4, 8].

A still controversial issue is the choice of the radioiodine activity to be administered at the time of ablation. ATA [1] and ETA [2] guidelines (dated 2009 and 2006, respectively) recommend the use of 30- to 100-mCi doses of radioiodine for low-risk patients and higher doses (>100 mCi) for high-risk patients. However, such indications are not based on strong clinical evidence but rather on expert opinion derived mainly from retrospective uncontrolled studies. Only recently, two large prospective, randomized, multicenter studies, one in France [9] and one in the UK [10] simultaneously published in the New England Journal of Medicine, compared the results of thyroid ablation performed after THW versus rhTSH and using 30 versus 100 mCi.
In both studies, inclusion criteria were: an age of 18 years or older; total thyroidectomy for differentiated thyroid carcinoma; tumor-node-metastasis (TNM) stage, ascertained on pathological examination of a surgical specimen, of pT1-T2 and any N stage (pT3 were also included in the UK study), and absence of distant metastasis. Thyroid ablation was assessed 6–9 months after RAI ablation by neck ultrasonography and measurement of rhTSH-stimulated Tg in the French study and, in addition, by diagnostic radioiodine WBS in the UK study.

In the French study [9], out of 684 patients with data that could be evaluated, ultrasonography of the neck was normal in 652 (95%), and the stimulated Tg level was ≤1.0 ng/ml in 621 of the 652 patients (95%) without detectable Tg antibodies. Thyroid ablation was complete in 631 of the 684 patients (92%). The ablation rate was equivalent between the iodine-131 doses and between the thyrotropin-stimulation methods.

In the UK study [10], data could be analyzed in 421 patients. Ablation success rates were 85.0% in the group receiving low-dose radioiodine versus 88.9% in the group receiving the high dose and 87.1% in the rhTSH group versus 86.7% in the group undergoing THW. All 95% CI for the differences were within ±10 percentage points, indicating noninferiority. Similar results were found for low-dose radioiodine plus rhTSH (84.3%) versus high-dose radioiodine plus THW (87.6%) or high-dose radioiodine plus rhTSH (90.2%). Of additional interest is the finding that the low-dose protocol was associated with fewer days of hospitalization and that the proportions of patients with adverse events were lower in the low-dose group versus the high-dose group and in the rhTSH group versus the THW group. As expected, symptoms of hypothyroidism and quality of life were significantly better in the rhTSH-treated groups.

The message of these clinical trials is very clear: low doses of radioactive iodine after preparation with rhTSH have similar ablation rates compared with high doses and THW, with the advantage of fewer side effects, shorter or no hospital stay, and better quality of life. Of course, the two studies cannot answer the question of whether the rate of recurrences in a long-term follow-up will be the same. However, based on retrospective available data showing that less than 1% of patients with low-risk cancer who had normal neck ultrasonography and an undetectable rhTSH-stimulated serum Tg level will have a clinical recurrence over a 10- to 15-year period [11–13], we can be confident that the long-term outcome of the patients enrolled in the French and UK studies will confirm their favorable outcome. While awaiting these results, my personal opinion is that whenever thyroid ablation is indicated in low- or intermediate-risk patients with differentiated thyroid cancer, the 30-mCi dose after preparation with rhTSH should be the standard of care.

Disclosure Statement

Dr. Pacini has been a consultant and acted as a lecturer for Genzyme.

References

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