Radiology: Imaging Cancer

COMMENTARY

Thyroid Nodule Ablation: Ever Expanding Indications

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Barry A. Sacks, MD, FSIR, was previously chief of interventional radiology at Harvard Medical Faculty Physicians and Beth Israel Deaconess Medical Center and is now retired. He was a pioneer in interventional radiology, a founder of the Society of Interventional Radiology, and a former president of the New England Society of Interventional Radiology. His clinical focus on endocrine diseases gained regional and national reputations, with expertise in petrosal vein, parathyroid vein, and adrenal vein samplings, as well as endovascular and direct access ablations (thyroid nodules, parathyroid adenomas, and aldosteronomas).

After 15 years of research and clinical practice pioneered in Europe and Asia, percutaneous thermal ablation for thyroid nodules is increasingly being performed in the United States. The focus of initial research and use is treatment of benign, symptomatic, or cosmetically unsightly nodules, as well as autonomously functioning nodules, supported by major societal guidelines (1).

Societal guidelines also support the use of thermal ablation for malignant thyroid nodules such as papillary thyroid microcarcinoma, unresectable thyroid cancer, neck lymph node recurrences, and distant metastases in appropriately selected patients. The indolent nature and very low recurrence and metastasis rates of incidentally found papillary thyroid microcarcinoma, coupled with fear, risks and cost of surgery, and active surveillance led to consideration of thermal ablation as an alternative option. Thermal ablation is less costly, and 5-year oncologic outcomes have been reported as similar to those of surgery, while eliminating hospital stay, risk of hypothyroidism, and neck scars (2).

If ablation outcomes can be comparable to surgery in cases of indolent thyroid cancer, a natural next step could be to investigate its use in nodules with low malignant suspicion or potential, namely, Bethesda III (atypia of undetermined significance) thyroid nodules. In this issue of *Radiology: Imaging Cancer*, Tang and Chen et al present a study of 95 patients with Bethesda III nodules who had a negative eight-gene panel mutation profile, treated with microwave ablation. Patients were observed for an average of 6.8 months, with 36 patients followed up for 1 year and 15 patients followed up for 2 years. There was no evidence of nodule regrowth or progression to cancer during follow-up. The incidence of complications was very low, and there was no significant change in thyroid hormone levels during follow-up; both of these findings were consistent with data from other thyroid nodule ablation indications (3).

The authors reported a mean nodule volume reduction of 91% 2 years after ablation. Although nodule volume reduction is a key determinant of treatment success in benign nodules that cause compression or cosmetic concerns, it is not such a helpful end point in malignant or potentially malignant nodules. For the latter, what really matters is that nodules do not grow further. Therefore, unchanged size can be equally as good as decreased size. Future studies may assess if there is any correlation or predictive value of volume changes with future cancer development or recurrence rates.

The authors also analyzed cosmetic improvement scores, which again are relevant when dealing with large volume, benign, symptomatic, or unsightly nodules, and not so relevant when dealing with atypical nodules treated because of their malignant potential rather than size or volume.

During submission and review of this study, two additional reports were published that focused on treatment of Bethesda III thyroid nodules with negative molecular testing results by radiofrequency ablation. The first study included a cohort of 33 patients; of those patients, 20 were followed up for 1 year and five for 2 years. Although the authors did not specifically report on progression to cancer rates, US imaging follow-up showed an average nodule volume decrease of 62% at 1 year and no complications (4).

The second study compared 18 patients with 20 Bethesda III nodules with negative molecular testing results to 174 patients with 230 benign nodules who were treated with radiofrequency ablation and observed for up to 1 year (median 6.9 months). Both groups showed similar rates of nodule volume decrease at 1 year (84% vs 78%). The mean thyroid-stimulating hormone levels remained in the normal range for all patients and there was no need for thyroid hormone supplementation. One patient in the Bethesda III group experienced regrowth of the treated nodule at 36 months, which was found to be a metastasis from urethral cell carcinoma. No complications were observed in the Bethesda III group (5).

Despite the short follow-up duration of the study by Tang and Chen et al, as well as the two aforementioned studies, these results are promising and exciting. Thyroid nodules are detected very often at physical examinations and imaging studies. Such

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detection leads to patient anxiety and the need for endocrinology referrals, follow-up imaging, and biopsies, all of which are costly and burdensome to both patients and health care systems. Although clearly benign or malignant nodules have fairly straightforward management pathways, atypical lesions of indeterminate significance are particularly bothersome to patients and clinicians. They account for up to 30% of biopsy results and carry a malignancy risk of around 22%. Although genetic molecular testing can improve the diagnostic accuracy for Bethesda III nodules, an uncomfortable degree of uncertainty always remains. The ability to treat them with a safe, fast, minimally invasive procedure that can put the matter to rest and obviate the need for surgery or additional follow-up and imaging is highly desirable. In addition, the ablation option allows for avoidance of scars and general anesthesia in combination with faster recovery time and return to daily activities.

Before this can become a new reality, however, additional studies with longer follow-up are necessary to confirm that ablated Bethesda III nodules with negative molecular profile do not recur or develop into cancer. Following that, the next frontier in the ever-expanding investigation of thermal ablation for thyroid nodules should be Bethesda IV nodules with negative molecular profile. Keep advancing!

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