Percutaneous Treatment of Benign Thyroid Nodules: Time to Bring It to the United States?

The current management of thyroid nodules is mostly directed at triaging nodules for a dichotomous outcome: nodules that must or should be surgically removed vs nodules that can be watched. Thyroid nodules concerning for malignancy are, for the most part, surgically removed as a way of improving life expectancy. However, some benign thyroid nodules, although not life-threatening, may cause undesirable compressive symptoms or cosmetic concerns. Thyroid surgery carries a small risk of complications, including damage to the recurrent laryngeal nerve (with consequent dysphonia), hypothyroidism, and a surgical scar. These risks are well accepted in the setting of a curative operation for malignancy, but the risk-benefit analysis is less clear when a benign condition, causing only subjective symptoms, is considered. In addition, patients with cosmetic concerns must trade a visible lump for a visible scar, a choice that may be challenging to some. In this issue of Mayo Clinic Proceedings, 2 studies from Mayo Clinic provide the first published US experience with 2 distinct, less invasive techniques in the treatment of benign thyroid nodules.

In the first study, Iñiguez-Ariza et al describe the use of percutaneous ethanol injection (PEI) for cystic nodules. In the second study, Hamidi et al report on the use of radiofrequency ablation (RFA) in the treatment of cytologically benign solid thyroid nodules. Both studies are retrospective and relatively small but are meritorious in that they bring to patients in the United States treatment options already available in other countries.

Iñiguez-Ariza et al describe treatment with PEI in 20 patients with either cystic or mostly cystic nodules, with median nodule shrinkage of 75% and a relatively low complication rate. Although this article does not describe the procedure in detail, it was presumably performed under local anesthesia.

In the study by Hamidi et al, RFA treatment of 14 patients with solid nodules resulted in resolution of compressive symptoms in 8 of 12 patients and improvement of cosmetic concerns in all 8 of them. The procedure was completed in 1 session for all the patients and resulted in virtually no complications of any significance. However, the procedure had to be performed under general anesthesia owing to concerns for possible complications related to patient motion. The median volume reduction of the nodules was 44%.

Percutaneous ethanol injection and, more recently, RFA have been used in Europe and Asia for decades, and the experience is well described in the literature. The procedures have been used in autonomously functioning solid thyroid nodules, nonfunctioning solid thyroid nodules, and cystic nodules. The overall volume reduction ranges from 40% to 70%, with excellent effect on symptoms. No reports on these procedures has been published by centers in the United States until now. These therapeutic options are, thus, not available to most patients in the United States.

The 2 techniques described in this issue of the Proceedings are quite different in nature if not in goals, and this is reflected in the different choices made by the authors of the present articles in treating the 2 different types of nodules: RFA induces thermal injury to the tissue via concentrated transfer of energy, whereas ethanol causes protein denaturation and necrosis of thyroid cells, stroma, and microvasculature; RFA requires costly equipment, whereas PEI requires only basic supplies; and RFA is a lengthier procedure and requires a larger (18-gauge) needle than PEI but delivers its effect with controllable radius and energy; in contrast, the distribution of...
ethanol, and, therefore, its concentration in and around the target lesion, is somewhat unpredictable. Given its unpredictability, PEI may require multiple sessions to safely achieve its goals when applied to solid nodules, whereas a single longer session is typically used with RFA. With cystic nodules, however, the amount of tissue needing treatment is much smaller as this involves the thin cyst wall and variable amounts of solid tissue after removal of the cystic fluid. Therefore, in cystic nodules a single PEI session is most often effective, with the possible exception of large, multilocular nodules. A recent randomized clinical trial showed no superiority of RFA over PEI in the treatment of predominantly cystic nodules, both in terms of efficacy (87% vs 82% volume reduction, respectively) and safety. Given the greater convenience and lower costs, PEI seems to be the treatment of choice for cystic nodules, justifying the choice made by Iniguez-Ariza et al. Head-to-head comparisons of the 2 techniques for solid nodules are not available, but several studies suggest lower efficacy and higher risk of relapses with PEI in solid nodules. The American Association of Clinical Endocrinologists guidelines, which were formulated largely by a collaboration of American and Italian thyroidologists, suggest that PEI is limited to and preferred for cystic nodules, whereas RFA or laser thermal ablation is used with solid nodules; this guideline is followed by Hamidi et al. in the second article in this issue of the Proceedings. The latest edition of the American Thyroid Association guidelines takes into consideration only PEI as an option for cystic nodules and offers surgery only for benign solid nodules causing compression or cosmetic discomfort.

The safety profiles for the procedures undertaken in these 2 US studies are excellent, with no major adverse events. However, some caution is advisable. In a recent multicenter study of RFA, the incidence of major complications was 1.4%, with transient voice changes in 15 of 1459 patients but no cases of permanent recurrent laryngeal nerve injury; this is still a very favorable safety profile.

Given the data presented, should these techniques be used more often and widely in clinical practice in the United States? The answer is probably yes because they provide a valid alternative to surgery for patients who seek resolution of their symptoms but who either do not wish or are unable to tolerate surgery. However, some guidelines should be followed, and additional questions need to be answered by continued research.

These procedures should be performed only by clinicians with extensive experience in neck imaging and in the management of thyroid nodules. Many of the leading international centers in this field offer short training courses, which is an excellent way to ascend the learning curve without putting patients at risk. Endocrinologists should enroll the help of interventional radiologists with experience in the ablation of other masses, especially if RFA is being used. Although there may be significant expertise in community centers, these procedures would best be performed in tertiary centers, which are more likely to acquire the necessary experience. Patients for whom these techniques are offered should be carefully selected. Exclusion of malignancy with fine-needle aspiration is clearly very important. Ongoing monitoring after the procedure is also recommended because a small risk of false-negatives with fine-needle aspiration biopsies is presently unavoidable. Compressive symptoms are difficult to measure objectively and can sometimes reflect anxiety immediately after learning of “a mass in my neck.” In these cases, a few months of observation before turning to ablation may sometimes lead to alleviation of these symptoms. The evidence favors the use of RFA for solid nodules, whereas ethanol should be used for mostly cystic nodules (RFA would be just as effective but more expensive).

Hopefully, in the future, additional research will answer some remaining questions. What is the long-term efficacy of these techniques? What is the long-term risk of relapses? What happens to the few false-negative malignant nodules, which inevitably will be inadvertently treated? What is the role of other methods, such as laser thermal ablation, microwave ablation, and others not yet available in the United States? Is general anesthesia needed for RFA?

For the time being, it seems appropriate to offer cautious encouragement to American
thyroidologists to consider percutaneous ablation for selected patients with symptomatic thyroid nodules.

Giuseppe Barbesino, MD
Thyroid Unit
Massachusetts General Hospital
Harvard Medical School
Boston, MA

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Correspondence: Address to Giuseppe Barbesino, MD, Thyroid Unit, Massachusetts General Hospital, Harvard Medical School, WACC 730S — 55 Fruit St, Boston, MA 02114.

REFERENCES