Thyroid Radiofrequency Ablation: From Basics to Updates

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Introduction

Thyroid nodules are a common clinical finding, which are found in 19-67% of patients. Although most thyroid nodules are benign and do not require treatment, some patients require treatment due to nodule-related symptoms and/or cosmetic problems. Although surgery is a curative method, there are drawbacks such as scar, general anesthesia, long recovery time, and hypothyroidism. Therefore, the use of radiofrequency ablation (RFA) on thyroid nodules has been first introduced in 2001. Since then, many clinical trials have shown that RFA is a good alternative to surgery in patients with benign thyroid nodules. Recent trials also have demonstrated that RFA of recurrent thyroid cancers may be an alternative to surgery in patients at high surgical risk and in patients with inoperable symptomatic recurrent cancers. The purpose of this article is to review the current evidences of thyroid RFA, focusing on its efficacy and safety, and to introduce the recent updates.

Indications

The consensus statement and recommendations for thyroid RFA have been initially reported by the Korean Society of Thyroid Radiology (KSThR) in 2012, and widely adopted from different authors and societies (1). In this guideline, RFA is indicated in patients with benign thyroid nodules who have symptoms and/or cosmetic problems and in patients with autonomously functioning thyroid nodules (AFTNs). RFA can be used in patients with recurrent thyroid cancers at high surgical risk and in patients who refuse to undergo repeated surgery. Nodules with a maximum diameter more than 2 cm that continuously grow are recommended as a possible indication based on symptoms and clinical concerns. However, ethanol ablation, rather than RFA, is recommended as the first-line treatment for cystic thyroid nodules since it showed similar efficacy and safety while requiring fewer treatment sessions and being more cost-effective. Two separate US-guided fine needle aspiration and/or core needle biopsy are recommended to confirm the nodules as being benign. Follicular neoplasms or primary thyroid cancers are not generally recommended for RFA.

Basic Techniques and Devices

Regarding the procedure, the 'trans-isthmic approach' and 'moving-shot technique' are

recommended as a basic technique for thyroid RFA (1, 2). After local anesthesia, the electrode tip is inserted through the isthmus into thyroid nodule along the short axis of the nodule, so called 'trans-isthmic approach' method. Then, thyroid nodules are ablated using a 'moving-shot technique'. In this technique, thyroid nodules are divided into multiple small conceptual ablation units and RFA is performed unit by unit by moving the electrode. RFA is terminated when all conceptual ablation units of the targeted nodule have become transient hyperechoic zones. A modified, straight-type, internally cooled electrode for thyroid RFA is short (7 cm) and thin (18-19G) for easy to control, with active tips of various sizes (0.5, 0.7, 1.0, or 1.5 cm). The RF power and size of active tip is decided depending on the size and the internal characteristics of the nodules. With 1 cm active tip, ablation is usually performed with 30–50 watts of RF power.

Recent Updates on Techniques and Devices

Regarding the techniques, two vascular ablation techniques, artery-first ablation and marginal venous ablation, have been proposed by Park et al (3). Since benign thyroid nodules are usually hypervascular, heat-sink effect interferes with complete ablation of the margin of the target nodule. Therefore, artery-first ablation technique can be applied to hypervascular thyroid nodules with prominent feeding artery. This technique ablates the main feeding artery as the first step, and can be easily applied to a nodule with a feeding artery entering through the isthmus. Marginal venous ablation technique is used for thyroid nodules with prominent marginal draining veins.

Regarding the devices, a new 3.8 mm electrode tip is developed for the treatment of smaller recurrent cancers. Small active tips allow a safe treatment with minimal tissue damage to the adjacent critical structures. New bipolar electrode simplifies the procedure without grounding pads and makes a safe treatment in pregnant women and in patients with implanted electrical devices (3). Virtual needle tracking system, proposed by Turtulici et al. (4), is helpful for less-experienced operators for continuous monitoring of the needle tip during the RFA. New unidirectional ablation electrode (270° of insulation) creates a half-moon-shaped ablation zone, which ablates tumors that are partially attached to a critical structure without causing thermal injury (5).

Current Evidences of Thyroid RFA

The efficacy of RFA could be evaluated by the volume reduction rate, therapeutic success rate, and changes of the symptomatic and cosmetic scores for benign thyroid nodules. Many clinical trials have demonstrated the mean volume reduction rate of 32.7–58.2% at 1 month and 50.7–84.8% at 6 months for RFA of benign thyroid nodules (6-10). Nodule-related symptoms and cosmetic problems are also significantly improved or disappeared in most patients. In a long term follow-up study, RFA was effective over a 4 year follow-up period with consistently decreasing the nodule volume until the last follow-up, up to 93.5%. A recent prospective multicenter study and international collaborative

trial generalized the efficacy and safety of RFA regardless of the operators or institution, when performed by well-trained operators using similar techniques and devices. A comparison study of RFA with surgery showed that RFA had advantages over surgery, in terms of fewer complications, preservation of function, and fewer hospitalization days although both were effective for treating benign thyroid nodules; therefore, they concluded that RFA should be considered a first-line treatment for benign thyroid nodules (11). A systematic review with meta-analysis, and indirect comparison study with laser ablation, also presented a strong evidence of RFA for benign thyroid nodules (12-14).

RFA for AFTNs showed volume reduction rates of 52.6 to 70.7% at 6 months, and improved or normalized thyroid function in most patients (15-17). In a multicenter study, hyperthyroidism caused by AFTN improved in all patients and completely normalized in 81.8% of patients; therefore, they concluded that RFA can be considered an alternative to surgery or radioiodine therapy. However, since untreated peripheral portions of AFTNs could interfere with improvements in thyroid function, complete ablation is required for AFTNs. A greater number of treatment sessions are usually required for AFTN than non-functioning nodules (2.2 versus 1.4) (17).

RFA also effectively controlled locoregional, recurrent thyroid cancers. The volume reduction rate was 56.0-95.1% and complete disappearance was 42.0–82.0% in previous studies. Serum thyroglobulin levels were also decreased after treatment in most patients and recurrences of the completely treated lesions were uncommon. Therefore, it was suggested that RFA may replace "berry picking surgery" in selected patients. RFA of inoperable patients with symptomatic, recurrent cancers resulted in a mean volume reduction of 50.9% and symptom relief in 63.6% patients (18, 19).

Complications of Thyroid RFA

The guidelines and previous studies including meta-analysis suggest that RFA is safe, well tolerated, and associated with a low incidence of complications (12, 20, 21). For benign nodules, the overall complication rate was 2.11% (95% CI: 1.15–3.06) and the major complication rate was 1.27% (95% CI: 0.81–1.73). For recurrent thyroid cancers, the overall complication rate was higher, 10.98% (95% CI: 4.82–17.15) and the rate of major complications of 6.71% (95% CI: 3.05–10.36). Various complications have been reported including nerve injuries (recurrent laryngeal nerve, cervical sympathetic ganglion, brachial plexus, and spinal accessory nerve), nodule rupture, permanent hypothyroidism as a major complication and hematoma, vomiting, skin burn, transient thyrotoxicosis, lidocaine toxicity, hypertension and pain as a minor complication. However, there were no life-threatening complications and the sequale rate was 0.21%.

Among the complications, the nerve injuries could be a serious problem in practice. Several nerves are located around the thyroid gland such as recurrent laryngeal nerve, vagus nerve, cervical sympathetic ganglion, cervical/brachial plexus, phrenic nerve, and

spinal accessory nerve, and they could be damaged during the procedure (22). Voice changes, by thermal injury to the recurrent laryngeal nerve or vagus nerve, are the most common major complication, reported to be approximately 1.0%. Horner syndrome by injury to the middle cervical sympathetic ganglion, tingling sense by injury to the brachial plexus, or drooping shoulder by injury to the spinal accessory nerve also have been reported after RFA of benign thyroid nodules and/or recurrent thyroid cancers. To prevent the nerve injuries, identification of a nerve by US and careful observation during the procedure is necessary; then, if the nerve is located close to the thyroid nodule, it is necessary to under-treat the nodule margin to prevent the nerve injuries. The 'trans-isthmic approach' and 'moving-shot technique' are helpful to prevent the nerve injuries.

Nodule rupture and hypothyroidism are rare, but possible complications. Delayed bleeding from intranodular microvascular leakage, post-procedural massage or movements of the neck are the causes of nodule rupture. Although conservative treatment without aspiration is usually enough for the treatment, surgical drainage could be required if the mass causes abscess formations. Regarding the hypothyroidism, patients with elevated thyroid antibodies before the treatment or patients with AFTN seems to have a higher risk for developed hypothyroidism after the treatment. Therefore, it is recommended to warn the patients with thyroid antibodies or the patients with AFTN about the possibility of hypothyroidism before the procedure.

Future Perspectives

Although thyroid RFA is proven to be safe and effective for benign thyroid nodules, surgery or radioiodine treatment is still widely used in practice. Prospective, randomized controlled trials are needed to compare the efficacy and safety of RFA with surgery or radioiodine treatment. Other nonsurgical treatments such as laser- or microwave-ablation have been also reported to be effective for thyroid nodules. Therefore, a direct comparison study with other nonsurgical treatments is required to establish a proper indication of thyroid RFA. How to select the best treatment modality among the different techniques has to be determined. The effect of thyroid RFA on thyroid-related quality of life should be validated in the future. Further researches are required for evaluating the potential role of RFA of primary thyroid cancer (papillary microcarcinoma), follicular neoplasm, and parathyroid adenoma in near future.

Conclusion

RFA is an effective and safe treatment option in patients with benign thyroid nodules who complain of symptoms and/or cosmetic problems and in patients with AFTN. RFA of recurrent thyroid cancers could be a possible option in patient with high surgical risks and in patients with inoperable symptomatic recurrent cancers.

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