Management of Benign Symptomatic Thyroid Nodules in Rhode Island Using Radiofrequency Ablation

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ABSTRACT

The management of benign symptomatic thyroid nodules can pose a challenge when weighing treatment options. While surgical resection has been the gold standard, the risks and consequences of partial or total thyroidectomy may outweigh the benefits of the procedure. Additionally, a significant number of patients are not surgical candidates due to comorbidities, potential risks, or personal preference. Radiofrequency ablation (RFA) has emerged as a minimally invasive, low-risk alternative to traditional surgery, and it has demonstrated to have high efficacy in nodule volume reduction, symptom resolution, and cosmetic improvement. Hence, the use of RFA for treatment of benign thyroid nodules has been supported by both international and national professional groups. This paper hopes to promote the use of RFA for treatment of benign solid thyroid nodules in the Rhode Island population as well as outline its potential clinical application.

KEYWORDS: Radiofrequency ablation; benign symptomatic thyroid nodule; minimally invasive procedure

INTRODUCTION

There is a high prevalence of thyroid nodules in the general population, with an upwards of 50–60% detection.[1] The majority of thyroid nodules are found from incidental findings and benign. Hence, management includes ruling out potential malignancy (5–15% of cases)[2,3] and treatment of nodules causing significant symptoms and/or cosmetic concerns. Symptoms of a thyroid nodule can include dysphagia, dyspnea, foreign body sensation, voice change, and cough.[4] In addition, toxic nodules producing hormone dysfunction and thyrotoxicosis are often an indication for treatment.

Surgical resection has been the gold standard for treatment of clinically significant benign thyroid nodules. Partial or total thyroidectomy poses certain risks and complications including transient hypocalcemia (~5–20%),[5] permanent hypocalcemia (<3%),[5] persistent hypoparathyroidism (~2%),[6] recurrent or superior laryngeal nerve injury (1–4%),[6] hemorrhage (~2%).[7] The incidence of post hemithyroidectomy hypothyroidism has been reported to be approximately 27%, indicating that a significant portion of patient will require thyroid hormone therapy.[8] These risks and complications often outweigh the benefits of the procedure, especially in patients with benign disease. Therefore, there has been an increased interest towards alternative minimally invasive procedures. Specifically, radiofrequency ablation (RFA) has garnered great interest due to its increased efficacy in comparison to other ablation treatments.[9]

RFA is a minimally invasive, low-risk procedure that utilizes an electrode under sonographic guidance to treat the target thyroid nodule. RFA has been endorsed in guidelines by multiple national, professional societies as a promising alternative to surgery for patients with benign symptomatic thyroid nodules and/or with malignant disease who are not surgical candidates.[1,10] International groups including the Korean Society of Thyroid Radiology and European Thyroid Association also share similar sentiments in recent guidelines for use of RFA for clinically significant benign thyroid nodules.[11-15] This article hopes to describe the potential impact of RFA as a low-risk and cost-effective alternative for the treatment of benign solid thyroid nodules in select patients in the state of Rhode Island.

CURRENT PRACTICE GUIDELINES

Various professional groups have supported the use of RFA for treatment of benign symptomatic thyroid nodules, and as such, there are agreements as well as variations in specific practice guidelines outlined. The Asian Conference on Tumor Ablation (ACTA) Task Force consolidated recommendations and highlighted areas of debate from recommendations made by academic societies in various countries.[13] For benign, nonfunctioning thyroid nodules with symptoms or cosmetic concerns, a 10 cm Visual Analog Scale for symptoms and cosmetic score (a cosmetic score of 1 to 4: (1) no palpable mass, (2) no cosmetic issues but a palpable mass, (3) cosmetic issue only during swallowing, and (4) nodule visible to the naked eye) can be utilized to assess patient burden and the need for treatment.[13] While there are no definitive cutoff values for nodule size, nodules exceeding a maximum diameter of 2 cm and demonstrating continued growth may be considered for RFA treatment if they pose symptoms, cosmetic and/or clinical concerns.[11] Historically, cytologically benign nodules of 4 cm or larger were recommended for surgical removal due to increased risk of

carcinoma development, structural and/or compressive concerns, as well as cosmetic concerns, but modern approaches rely more on assessment of symptoms and changes over time as smaller nodules can also cause concerns depending on nodule location and patient neck circumference.[11,16]

THE RADIOFREQUENCY ABLATION PROCEDURE

The thyroid nodule should be confirmed to be benign by at least two ultrasound-guided fine needle aspiration (FNA) or core needle biopsy (CNB) prior to RFA to prevent possible false-negative diagnosis of malignancy.[13] However, some guidelines believe a single diagnosis of a thyroid nodule with highly suggested benign features (isoechoic spongiform or partially cystic nodules with an intra-cystic comet tail artifact) is sufficient.[11] On ultrasound, the following are evaluated in detail to determine if the nodule may be suitable for RFA: nodule echogenicity, margin, vascularity, volume, and relationship of nodule to surrounding critical structure. The following labs are also reviewed: complete blood count, coagulation test, thyroid function test, and thyroid autoantibodies if thyroid function test abnormality is present.[13]

RFA procedure consists of inserting a probe connected to a generator producing a high-frequency current into the target nodules. The resulting heat produced due to the electrical current passing through a circuit with focal impedance (i.e., the target tissue) induces thermal injury and coagulative necrosis in the target tissue.[4] The procedure is generally performed under local anesthesia and real-time sonography guidance; general anesthesia is not recommended.[13] Treated areas will appear as mildly hypoechoic spots on ultrasound, demonstrating tissue vaporization. There are several important techniques employed with thyroid RFAs to reduce complications related to thermal damage to surrounding structures. First, hydro-dissection technique is used to protect adjacent surrounding structures of the neck. The hydro-dissection technique involves injection of either lidocaine or dextrose 5% in water in between the nodule and critical adjacent structures (e.g., carotid artery, recurrent laryngeal nerve), creating a margin of safety that prevents unintentional thermal damage.[11,17] Second, the "moving-shot" technique through the trans-isthmic approach has been employed to treat thyroid nodules, where the electrode tip is moved continuously to ensure adequate treatment coverage and adequate sonographic target visualization while preventing overtreatment of the peripheral margins.[13] The electrode needle can be inserted in the midline-to-lateral direction first at the deepest and most remote portion of the nodule, and then gradually moved backwards for best electrode visualization and control.[13]

Follow-up visits are recommended at one to three months for early exam of initial effects of ablation and for thyroid function analysis, at six and twelve months for assessment of volume reduction as this is where max nodule shrinkage is obtained, and at every six to twelve months thereafter to monitor for regrowth.[12,13] In certain cases, including marginal regrowth of the treated nodules, increase of 50% volume compared to minimum recorded volume, <50% volume reduction rate, or incomplete resolution of symptoms, additional rounds of RFA may be considered.

PATIENT SELECTION AND ELIGIBILITY

RFA should be used for the treatment of solid or majority solid benign thyroid nodules causing symptomatic, clinical, or cosmetic concern. RFA should not be performed on nodules with high-risk ultrasound features due to risk of harboring malignancy, and unnecessary treatment of asymptomatic benign nodules are discouraged.[12] RFA can be the treatment of choice for autonomously functioning thyroid nodules (AFTNs) in instances where the patient refuses both surgery and radioactive iodine treatment. Additionally, it can be considered for cases of AFTN in young patients due to the potential of a much longer period of hypothyroidism following RAI or surgery.[4] RFA has demonstrated to have lower efficacy in larger nodules, and therefore nodules >20 mL in volume are not recommended for RFA treatment.[11] Selected cases of malignant thyroid nodule, such as residual or recurrent disease after thyroidectomy can be considered for RFA after multidisciplinary discussion. Indications for RFA of malignant nodules rather than surgical resection may be appropriate in cases where the patient is a nonsurgical candidate and the tumor is of specific locations (unifocal disease, central location in gland, confined to thyroid gland) or types.[4,10] Bipolar electrode may be recommended for pregnant women or patients with cardiac pacemaker.[13] Imaging from a benign thyroid nodule RFA procedure at Roger Williams Medical Center is shown in **Figure 1**.

OUTCOMES OF THYROID NODULE RADIOFREQUENCY ABLATION

Benign thyroid nodules compromise a high impact area of RFA. RFA has been widely adopted across Asia and Europe over the past decade for treatment of benign nodules. In international studies, there is an overall consensus in the literature suggesting RFA to be efficacious in reducing nodule volume, with 70% to 80% reduction in six to 18 months or even higher depending on the study, as well as improving related symptoms and cosmetic concerns.[18-22] Therapeutic response is often defined as >50% volume reduction after twelve months. A retrospective cohort study comparing outcomes of RFA to surgery for treatment of benign thyroid nodules found that RFA reduced nodular volume by 70% after 12 months and was more cost-effective than surgery for the treatment of nodule-related clinical problems.[22] A large systematic review of reports published between 2009 and 2021 of mostly solid nodules found that volume reduction at

Figure 1A,B. Pre-procedure imaging of a 2.9 x 2 x 2.8 cm TIRADS 4 right thyroid nodule with two fine needle aspiration results showing benign findings. Patient had symptoms of dysphagia and cosmetic concerns.

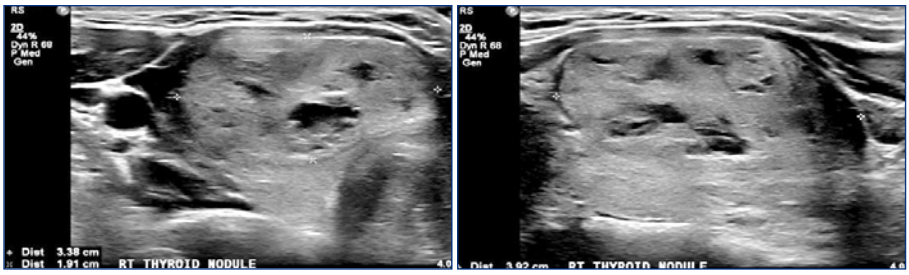
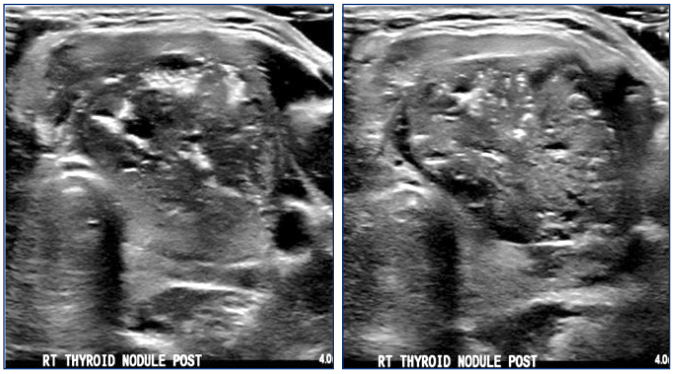


Figure 1C,D. Post-procedure imaging demonstrating post radiofrequency ablation changes including areas of hyperechogenicity without evidence of immediate complications.



12 months follow-up ranged from 67 to 75% for single treatment nodules and reached approximately 94% for repeat treatments, demonstrating that RFA produced long-term clinical efficacy.[18]

The FDA-approved use of RFA in soft tissue tumors in 2018, and since US-based studies have also found RFA to be efficacious in treatment of benign thyroid nodules. For large benign thyroid nodules, defined as 3 cm in largest diameter, an early case series by Mayo Clinic found a median volume reduction rate (VRR) of 44.6% over a median follow up of 8.6 months.[23] Subsequent studies in the US also found significant VRRs and good efficacy. A single center retrospective study between 2018 and 2021 found that mean VRR was 70.8% after a median follow-up period of 109 days, with symptomatic and cosmetic improvement ($P < 0.01$).[24] Both nonfunctioning thyroid nodules (NFTNs) and AFTNs were included in the study, and RFA was found to cause a greater volume reduction in smaller nodules ($P = 0.03$) and improve thyrotropin (TSH) in AFTNs (P value < 0.01).[25] A study at Columbia University saw that RFA procedures performed in the outpatient setting under local anesthesia were well tolerated and resulted in a VRR of 52.9% at one month follow-up.[21] All patients included in the study (n = 15), except two, had nodules that were benign on fine-needle biopsy but enlarging, symptomatic, or toxic, and patients were euthyroid at follow up, suggesting reduced need of thyroid hormone supplementation compared to traditional surgery.[8]

Several studies have also reported on the positive improvements of cosmetic and symptoms scores following RFA. A US-based study following 56 patients with 76 benign thyroid nodules treated with RFA demonstrated a significant improvement for goiter symptoms, anxiety, appearance, and quality of life at 12-month follow-up ($P< 0.05$).[26] Additionally, in a cohort of 94 elderly patients with cytologically benign compressive thyroid nodules, relief of compressive symptoms were found in 88% of patients.[27] Pooled measures of mean symptomatic score and cosmetic score from 14 and 12 available studies, respectively, demonstrated a decreased postoperative symptomatic score (3.83 vs 1.09) and cosmetic score (3.43 vs 1.51), providing further support for the efficacy of RFA in treating benign thyroid nodules for symptomatic and cosmetic indications.[11]

RFA is predominantly indicated for solid or predominantly solid benign thyroid nodules. Moderate efficacy has been demonstrated by RFA in treating toxic thyroid nodules with a 57% TSH normalization rate and 79% VRR at one year.[28] Other nodule subtypes including benign AFTNs, cystic nodules and malignant nodules may not be as effectively resolved with RFA compared to current standard treatments (e.g., RAI, ethanol ablation, surgery, respectively) and should only be treated in the case that the patient denies or is unsuited for surgery or RAI, or where the risks of hypothyroidism may be too detrimental.[4,11,12,19] While RFA and ethanol ablation have been demonstrated to have similar outcomes, the lower cost and superior safety profile of ethanol ablation indicates it as the preferred treatment for cystic nodules.[4]

SAFETY AND OTHER CONSIDERATIONS

RFA is generally well tolerated with low complications rates of around 3.3%.[29] Minor complications can include mild hematoma, postoperative transient hoarseness, mild pain, and skin burn; major complications, although rare, can include permanent voice change, brachial plexus injury, recurrent laryngeal nerve injury, nodule rupture, and permanent hypothyroidism.[29,30] However, generally when compared to surgery, RFA produces significantly lower incidence of complications than surgery (6.0% vs 1.0%, P= 0.002), lower rates of residual nodules (11.9% versus 2.9%, P = .004), reduced hospitalization days, and preservation of thyroid function.[24] Following RFA treatment for benign NFTNs, it has also been shown that while there is transient relative hypothyroidism and increase in thyroid antibodies,

the levels normalize within 12 months with most rises in TSH remaining in normal range.[31] Long-term follow-up will be necessary to monitor potential regrowth.

Multiple factors including ill-defined margins, large nodule size, functional autonomy, and low applied energy can affect the successfulness of RFA treatment as well as potentiation for nodule regrowth after treatment.[12,22] Regrowth rates can range from 0–34%, as demonstrated by a recent systematic review of data published between 2008 and 2021.[18] There is also reduced efficacy of RFA in larger nodules (>20 mL) and variable rate of thyroid function normalization for AFTN.[11] In past studies following patients treated for non-functioning thyroid nodules with RFA for over three years, 24–60% of cases required more than two sessions of RFA to maintain long-term volume reduction.[11] Therefore, while RFA causes expected decrease in nodule size, patients should be informed that there is not complete disappearance of the nodule and additional treatment or surgery may be necessary if there is subsequent regrowth.[13]

CONCLUSION AND LOOKING FORWARD

Radiofrequency ablation is an attractive alternative to conventional surgery for the treatment of benign thyroid nodules. With low complication rates, short procedure and recovery time, reduced cost, and efficacy in treating symptomatic benign thyroid nodules, it can serve as a great option for patients who are not great surgical candidates or who refuse surgery. RFA also greatly diminishes the risk of hypothyroidism and need for life-long hormone supplementation. Patient workup includes diagnostic thyroid ultrasound, clinical work up, and fine needle aspiration to rule out potential malignancy. Treatment of thyroid nodules posing no symptomatic or aesthetic concerns is not advised. With the proven safety and efficacy of RFA for treatment of benign thyroid nodules, we believe that this technique would be a great treatment option for patients in the state of Rhode Island.

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