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Clinical Research Article

Outcomes of Radiofrequency Ablation for Autonomously Functioning Thyroid Adenomas—Mayo Clinic Experience

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Abstract

Background: Autonomously functioning thyroid nodules (AFTNs) constitute 5% to 7% of thyroid nodules and represent the second most common cause of hyperthyroidism following Graves' disease. Currently, radioactive iodine (RAI) and surgery are the standard treatment options, and both incur a risk of postprocedural hypothyroidism and other surgery and radiation-related complications.

Methods: This work aimed at assessing the efficacy of radiofrequency ablation (RFA) as an alternative treatment option for resolving hyperthyroidism and the nodule volume rate reduction (VRR) and its associated adverse events.

Results: A total of 22 patients underwent RFA for a solitary AFTN. Seventy-two percent (n = 16) had subclinical hyperthyroidism, 9% (n = 2) had overt hyperthyroidism, and 18% (n = 4) were biochemically euthyroid on antithyroid medication. Average pretreatment TSH was 0.41 mIU/L (SD = 0.98) and free T4 1.29 ng/dL (SD = 0.33). Following a single RFA session, hyperthyroidism resolved in 90.9% (n = 20) and average VRR (61.13%) was achieved within 3 to 6 months following the ablation. Except for 1 nodule, none of the nodules grew during the follow-up period (16.5 months). Two patients (9%) developed transient tachycardia requiring short-term beta-blocker therapy, and 2 developed mild hypothyroidism requiring levothyroxine therapy. Two patients developed recurrent hyperthyroidism and elected to undergo lobectomy and repeat RFA respectively. No serious adverse effects were noted in this cohort.

Conclusion: RAI and/or surgery represent the standard of care for toxic adenomas, but RFA shows excellent efficacy and safety profile. Therefore, at centers with RFA expertise, it should be considered an alternative treatment strategy, avoiding radiation and surgery-related complications.

Key Words: thyroid nodule, hyperthyroidism, radioactive iodine, autonomous, radiofrequency, ablation

Thyroid nodules are extremely common with an estimated prevalence increasing with age, from 19% to 67% [1, 2]. While the majority of thyroid nodules are nonfunctioning, approximately 5% to 7% of nodules are autonomous in pediatric and adult populations and are termed autonomously functioning thyroid nodules (AFTNs) [3-8]. AFTNs combined with toxic multinodular goiters (TMNG) represent the second most common cause of hyperthyroidism in the United States, following Graves' disease [9, 10]. The American Thyroid Association recommends treating AFTNs due the association of the underlying hyperthyroid state (including subclinical hyperthyroidism) with adverse skeletal and cardiovascular complications [10]. In addition, treatment is also recommended at times for managing compressive symptoms caused by large AFTNs or TMNGs.

Currently, radioactive iodine (RAI) and surgery (either total thyroidectomy or lobectomy) are the approved treatment options for AFTNs. Both options are extremely effective in curing the underlying hyperthyroid state, but both procedures are associated, to a variable degree, with permanent postprocedural hypothyroidism [10]. To overcome this permanent adverse effect, additional therapies have been explored over the last 30 years [11, 12]. Antithyroid drugs (ATDs) have been utilized in the treatment of TMNG, but this would imply lifelong therapy [10]. Image-guided thermal ablation techniques (employing either hyperthermia or hypothermia) have been effectively utilized in the treatment of various tumor types over the years. Radiofrequency ablation (RFA), a form of hyperthermic ablation, has been shown to induce significant volume reduction for large nontoxic thyroid nodules [13]. Within the past decade, a few centers across the globe have utilized RFA for the treatment of AFTNs with the goal of avoiding both permanent hypothyroidism and possible surgical complications. This approach has shown promising results in resolving hyperthyroidism and achieving euthyroidism (67% of patients) along with a volume reduction rate (VRR) of 52% to 86% at 6 to 24 months postprocedure. Fortunately, only infrequent minor complications have been associated with this procedure [2, 3, 9, 14-19].

In the United States, RFA has been widely used to treat benign and malignant tumors of the bone, liver, and kidney, among other targets but only over the last decade has been utilized for the treatment of benign thyroid nodules [13]. The main thrust of its use is to decrease thyroid nodule volume and

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eliminate compressive symptoms. On the other hand, reports on its efficacy in controlling the hyperthyroidism associated with AFTN in the United States are sparse. Convinced of the benefits of RFA with volume reduction of benign thyroid nodules, we explored its utility in AFTNs with the primary goal of achieving resolution of hyperthyroidism. We present the outcome data of a single-center experience with the use of RFA as an alternative treatment modality for AFTNs.

Materials and Methods

Our retrospective study aimed primarily to assess RFA efficacy in resolving hyperthyroidism in patients with AFTNs. In addition, we analyzed the changes in volume post-RFA and evaluated the adverse events associated with the procedure. Further, we sought to explore the factors associated with positive response to treatment (resolution of hyperthyroidism and VRR > 50%).

Informed consent for RFA was obtained from all patients prior to the procedure. Following the approval from the Mayo Clinic Institutional Review Board, medical records of all patients who approved the use of their records for research and were treated with RFA for AFTNs between December 2013 and December 2021 were reviewed retrospectively. The data pertaining to the technical details of the procedure along with clinical, biochemical, and imaging follow-up were extracted and analyzed. The diagnosis of AFTN was confirmed if patients (1) had a thyroid nodule on the ultrasound (US) that (2) correlated with an increased uptake on RAI scintigraphy and (3) had a suppressed TSH with normal or elevated free T4 and total T3 (prior to any therapy including ATDs). All patients were presented with standard therapeutic options of both surgery and RAI ablation therapy. If both were unacceptable (personal choice and/or medical reasons), RFA was discussed. If deemed clinically appropriate and technically feasible, the nodules were considered further for RFA. All nodules of very low suspicion for malignancy based on ultrasound characteristics were offered to proceed directly to RFA. All other nodules were evaluated by fine-needle aspiration cytology. If benign, the patients were offered RFA. Patients who were diagnosed with hyperthyroidism secondary to TMNG or had other concurrent nontoxic nodules suspicious for malignancy were excluded.

The measurement of nodule volume, the assessment of the nodule's cystic content and its grading, as well as the assessment of the vascularity of each nodule and the grading of vascularity were performed as described in Supplementary Data 1 [20]. The severity of compressive symptoms and cosmetic complaints were collected before and after the procedure and were classified and assessed using the symptom score (SYS). Three parameters—Pressure symptoms, dysphagia, and esthetic complaint—were assessed based on severity and given a score from 0 to 2 (0 = absent, 1 = mild to moderate, 2 = severe). The sum of the 3 scores denoted the SYS, ranging from 0 to 6 [21].

The procedure was performed in interventional radiology by a team with extensive expertise in performing percutaneous thermal ablations. The procedural protocol involved using US guidance (GE LOGIQ E9, GE Healthcare, Chicago, IL, or Philips EPIQ, Philips Healthcare, Andover, MA) using an STARmed VIVA RF generator with fixed linear 18-gauge electrodes with active tips ranging from 0.7 to 1 cm. All patients received monitored anesthesia care or general anesthesia for the procedure. Further technical details are provided in the Supplementary Data 1 file [20]. A preablation plan was formulated for each nodule to determine the safest needle path and trajectory that would both avoid traversing critical structures (such as superficial veins) and allow electrode movement within the nodule with a single percutaneous access site. Often, this was performed as a trans-isthmic approach but not always. A combination of moving shot technique and overlapping ablations were performed [22, 23]. Given the emphasis on correcting the hyperthyroidism, the RFA procedure placed the emphasis on the most functional areas within the nodule, based on iodine scan and US Doppler information.

Complications were assessed during and immediately after the procedure. If the patient experienced any pain during the procedure, the ablation was paused while additional local anesthetic or additional sedation was administered. After a successful completion of RFA ablation, patients were monitored in the postprocedure care unit for 30 minutes (moderate sedation and local anesthesia) to 2 hours (general anesthesia patients).

Follow-up laboratory tests (TSH, free T4, and total T3) were performed at a minimum of 4 weeks and 6 months post-RFA and yearly thereafter. Comprehensive clinical examinations and imaging were typically performed at 6 months post-RFA and yearly thereafter for a few years. On US examinations, changes in the largest diameter, nodule volume, and vascularity were assessed and compared to pre-RFA appearance. The VRR was calculated using the following equation: VRR (%) = [(Initial volume (ml)—Final Volume (ml))×100]/Initial volume [24, 25]. Symptoms and cosmetic scores were evaluated at each follow-up, and the scores were compared to the preablation assessment.

Statistical Analysis

We performed descriptive statistics on the clinical, biochemical, and imaging variables (thyroid nodule size and volume). Categorical variables were described in percentages whereas continuous variables expressed as median with interquartile ranges (IQRs).

Results

Baseline Characteristics

Over the period described, we identified 22 toxic nodules that underwent RFA in 22 patients (77% women). The average age was 52.1 years (SD: 14.62; IQR: 31-72 years) and average body mass index 27.4 kg/m^2 (SD: 4.67; IQR: 19.35—38.45 kg/m^2) (Table 1).

Thyroid Status and Prior Treatment

At the time of RFA therapy, 9.1% (n = 2) of our cohort had overt hyperthyroidism, 72.7% (n = 16) had subclinical hyperthyroidism, and 18.2% (n = 4) were euthyroid while being on an ATD prior to RFA treatment. One patient (4.5%) had prior radioactive iodine treatment, but thyrotoxicosis persisted. The average pretreatment TSH was 0.41 mIU per L (normal range: 0.3- 4.2 mIU/L; SD: 0.98), and the average pretreatment free T4 was 1.29 ng/dL (normal range 0.9-1.7 ng/dL; SD: 0.33).

Thyroid Nodule Structure

Each patient had a single nodule identified as toxic based on the imaging studies (US nodule corresponding with increased uptake of radioiodine in the presence of suppressed serum TSH levels). The average pretreatment volume of the thyroid

Table 1. Patient baseline characteristics

Total number of patients	22
Average age	52.1 [(52.1 ± 14.6); range: 31-72]
Median age	56.29
Sex (F:M)	17:5 (77% F and 23% M)
Average BMI (kg/m^2)	27.4 [(27.4 ± 4.67); range: 19.35-38.45]
Average preablation volume, mL	12.29 [(12.29 ± 10.81); range: 0.5-37.48]
Average TSH (mIU/L)	0.41 [(0.41 ± 0.98); range: 0.001-4.2]
Average free T4 (ng/mL)	1.29 [(1.29 ± 0.33); range: 0.8-2.3]
Thyroid function status	16 (72.7%), subclinical hyperthyroid 2 (9.1%), overtly hyperthyroid 4 (18.2%), euthyroid on ATD
Radioactive iodine uptake and scan	100% (solitary hot nodule)
Previous therapy prior to RFA (%)	
ATD	4/22 (18.2)
Radioactive iodine	1/22 (4.5)
None	17/22 (77.3)
Symptoms score (%)	
Absent	13/22 (55.5)
Mild	5/22 (22.7)
Moderate	1/22 (4.5)
Severe	3/22 (13.6)
Nodule characteristics (cystic component) (%)	
<10%	10 (45.4)
10-25%	7 (31.8)
25-50%	3 (13.6)
>50%	2 (9.1)

Abbreviations: ATD, antithyroid drug; BMI, body mass index; F, female; M, male; RFA, radiofrequency ablation.

Table 2. Comparison of thyroid function and nodule characteristics pre- and post-RFA

	Pre-RFA	Post-RFA
Total number of patients	22	22
Average TSH (mIU/L)	0.41 [(0.41 ± 0.98); range: 0.001-4.2]	1.82 [(1.82 ± 1.9); range: 0.03-6.9]
Average T4 (ng/mL)	1.29 [(1.29 ± 0.33); range: 0.8-2.3]	1.02 [(1.02 ± 0.2); range: 0.8-1.2]
Average volume, ml	12.42 [(12.29 ± 10.81); range: 0.5-37.48]	4.5 [(4.5 ± 5.1); range: 0.16-21.42]
Average symptom score	0.73	0.05
Rate of hyperthyroidism resolution (%)	N/A	91
Volume reduction rate (%)	N/A	61.13

Abbreviation: RFA, radiofrequency ablation.

nodule was 12.42 cm^3 (SD: 10.81; IQR: 0.5-37.48 cm^3) (Table 2). All toxic nodules had both solid and cystic components. Seventeen patients (77.3%) had a cystic component up to 25%, while 2 patients (9%) had a cystic component larger than 50% (Table 1). Based on indeterminate ultrasound appearance, 14 patients (63%) underwent a fine-needle aspiration of the toxic nodule that confirmed its benign character.

Thyroid Function Post-RFA

After a single session of radiofrequency ablation, the TSH normalized in 90.9% (n = 20) patients within 3 to 6 months following the RFA. In our cohort, the TSH remained normal throughout the follow-up (average follow-up duration 16.5 months, SD = 11.80). (Fig. 1) The average TSH during the last follow-up was 1.82 mIU/L (SD: 1.9), significantly different compared to baseline ($P < .05$), and the average free T4 was 1.02 ng/dL (SD: 0.2, $P = .059$ for comparison with baseline). Two patients (9.1%) developed mild hypothyroidism requiring a small dose of levothyroxine replacement therapy. All 4 patients on an ATD prior to the RFA discontinued this therapy within 3 months after the procedure, and their biochemical parameters remained normal during the follow-up. Two patients (9.1%) had persistent or recurrent hyperthyroidism. One did so 45 months after the RFA procedure (euthyroid until then, after a single RFA session). The autonomously functioning dominant nodule started regrowing (+13.8% compared to baseline ultrasound), and the patient decided to undergo lobectomy. The other patient had persistent hyperthyroidism (18 months after the first RFA), despite decreasing volume (22% VRR). Repeat RAI uptake scan showed the same dominant thyroid hot nodule, and the patient underwent repeat RFA safely and effectively, without any complications.

Thyroid Structure Post-RFA

The median volume decreased by 56.8% by 1 to 4 months (IQR: 21.74-77.1%; n = 10) and by 63.7% by 5 to 8 months (IQR: 29.02-84.9%; n = 8) without significant changes thereafter (see Fig. 2). The average VRR (61.13%) was achieved within 3 to 6 months following the RFA and, importantly, during the follow-up period, except for 1 nodule, none of the nodules grew. The average volume of the nodules during the last follow-up was 4.5 cm^3 (SD: 5.13, $P < .05$ compared to baseline).

Compressive Symptoms and Aesthetic Concerns

Nearly half the cohort (n = 9, 40.9%) had some form of complaints secondary to the nodule, either pressure symptoms (eg, dysphagia) or esthetic concerns. Among these, based on the SYS, 18.2% (n = 4) had moderate to severe complaints with a SYS of ≥2 and 22.7% (n = 5) had mild complaints with SYS of 1. The average SYS prior to the RFA treatment was 0.73 (SD = 1.08). Following a single session of RFA treatment, 95.4% (n = 21) had complete resolution of their symptoms with an average SYS of 0.05 (SD = 0.24, $P < .005$) after 3 to 6 months follow-up. Their SYS remained low during the period of follow-up.

Factors Predicting RFA Response

Given that the vast majority of our study subjects responded well to the RFA (21 out of 22 had resolution of hyperthyroidism within 3 to 6 months of the initial procedure), we were unable to assess any clinical, structural (eg, cystic content, vascularity), or biochemical parameters (eg, thyroid levels, antithyroid antibodies) that predicts better RFA outcomes.

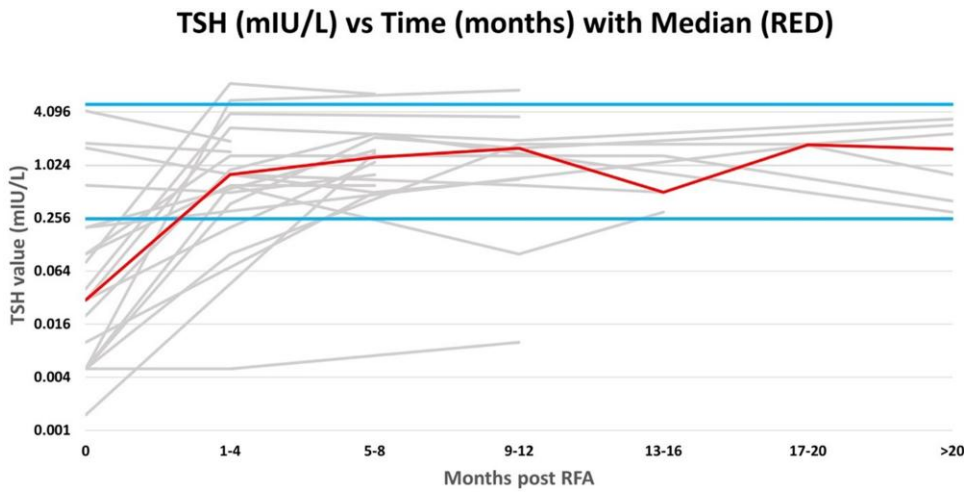

Figure 1. TSH (mIU/L) vs time (months). Change in TSH (mIU/L) over time in months following a single radiofrequency ablation session with the median TSH represented in solid bold undulating line and the bold parallel lines representing normal TSH range.

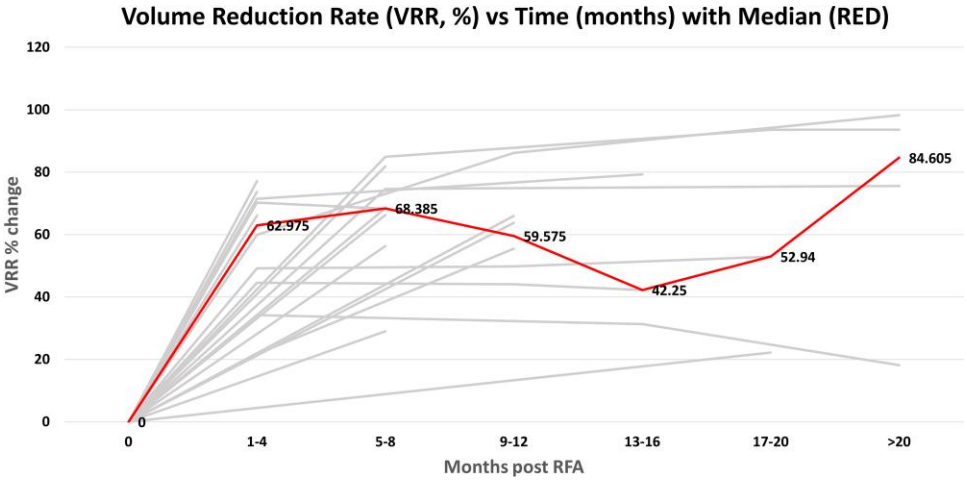

Figure 2. VRR (percent) vs time (months). Change in VRR (percent) over time in months following a single radiofrequency ablation session with the median VRR (percent) represented in solid bold undulating line.

Abbreviations: VRR, volume reduction rate.

RFA Safety Profile

Of the 22 patients who underwent RFA, 2 patients (9.1%) developed symptomatic tachycardia following the procedure that led to an emergency room visit and were treated with beta-blockers. This complication was transient, and neither of the patients required long-term treatment with beta-blockers. These two episodes could be related to transient thyrotoxicosis post-RFA. Fortunately, no patients developed hematoma, neck pressure, or pain beyond the first 3 days after the therapy. All local discomfort was managed well with over-the-counter analgesics following the RFA procedure.

RFA Insurance Coverage

This has been a concerning aspect for us and many other practitioners at other institutions. We have looked at the source of payments related to the procedure and were able to retrieve that data for 20 of our 22 patients. Only 1 patient in these 20 had a complete denial by their insurance company and further financial arrangements had to be made. All the other 19 patients for which data was available had their insurance provider cover the costs of the procedure.

Discussion

While many studies have focused on RFA for the management of nontoxic and large nodules with compressive symptoms, here we focus exclusively on its impact on toxic nodules. This topic is addressed less frequently in the literature and has limited data in the US population [9, 13]. We provide a comprehensive description of 22 patients who underwent RFA treatment for AFTN at our institution. While the overall number of patients is small, it is in line with the average of 24 patient/study reported elsewhere (range 9-40, Table 3). Ours is the first paper that looks carefully at the timing (3-6 months) of the hyperthyroidism resolution (90.9%) following a single RFA treatment, with excellent safety data and good VRR (61.1%). While compressive and esthetic concerns were less prominent in this series, there was also an overall improvement in patient symptoms as evaluated based on SYS.

Table 3. Literature review and comparison

Study	Year	Study design	Total no. of pts	Mean age	Previous Tx	Nodule characteristics	Electrode type	Technique	Type of anesthesia	Total no. of sessions	Mean f/u (months)	Average VRR	% Hyperthyroidism resolution (last f/u)
Baek et al	2008	Retrospective	9	47	None	Solid/mixed/cystic	17-G and 18-G	Moving shot	Local	1-4	6	70.70%	56%
Deandra et al	2008	Prospective	23	67	None	Solid/mixed	14-G	n/a	Local	1	6	50.70%	24%
Spiezia et al	2009	Prospective	28	72.5	Surgery (9); RAI (12)	Solid	14-G	n/a	Local	1-3	24	79.40%	79%
Faggiano et al	2012	Prospective	10	58	Surgery (2); RAI (2)	Solid	14-G	n/a	Local	1	12	86%	40%
Sung et al	2015	Retrospective	44	43	None	Solid/mixed	18-G	Moving shot	Local	1-6	6	74.50%	82%
Bernardi et al	2017	Prospective	30	69	None	Solid/mixed	18-G		Local	1	12	75%	50%
Dobnig et al	2018	Prospective	32	52	None	Solid/mixed	18-G	Moving shot	Local	1	3-12	N/A	84.30%
Casareo et al	2018	Prospective	29	51	None	Solid	18-G	n/a	Local	1	24	84%/68%	66%
Cervelli et al	2019	Retrospective	22	57.2	ATD (13)	Solid/mixed	18-G	Modified moving shot	Conscious sedation	1	12	76.40%	91%
Cappeli et al	2019	Retrospective	17	45.3	ATD (3/17)	n/a	19-G	Moving shot	Conscious sedation	1	12	72.90%	94%
Hussain et al	2021	Retrospective	20 (9-single)	42	ATD (8)	n/a	18-G	Moving shot	Conscious sedation + LA	1 (1 pt had 2)	n/a	71.10%	75%
Average												72.97%	67%
Mayo Clinic	2023	Retrospective	22	52.1	ATD (4); RAI/LT4 (1)	Solid/mixed	17/18-G	Moving shot	General	1 (1 pt had 2)	16.5	61.13%	91%

Abbreviations: ATD, antithyroid drug; f/u, follow-up; G, gauge; LA, local anesthesia; LT4, levothyroxine; n/a, not available; RAI, radioactive iodine; TFT, thyroid function test; Tx, treatment; VRR, volume reduction rate.

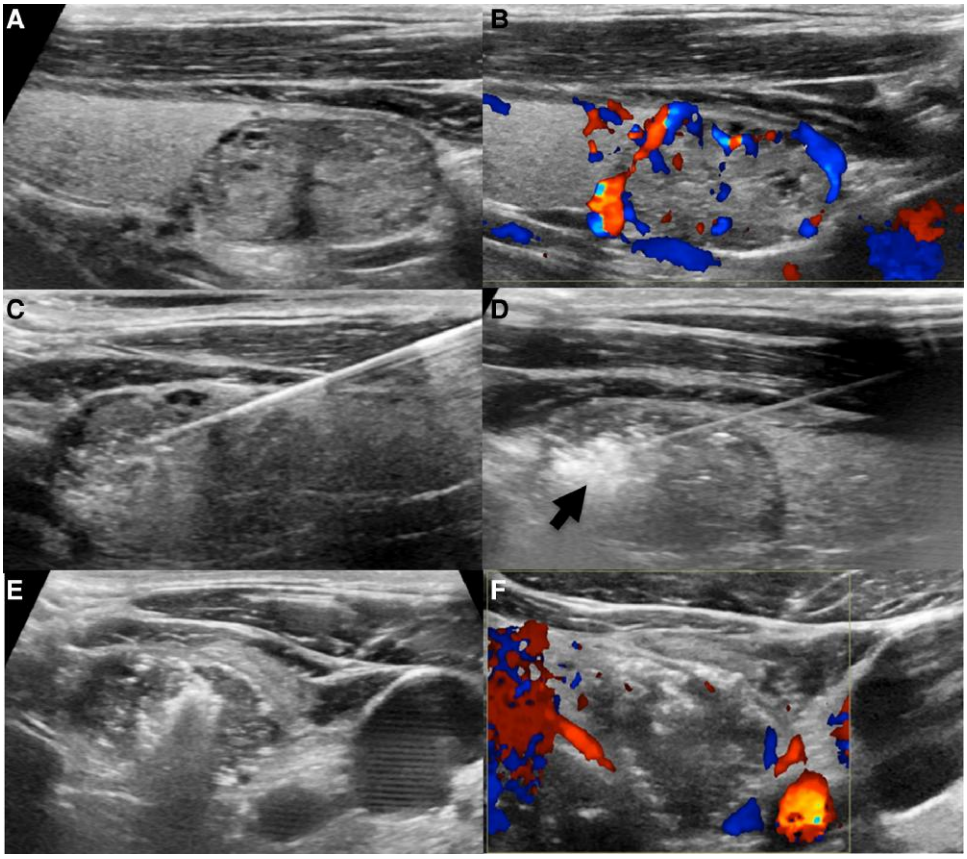

Figure 3. Radiofrequency ablation procedure of one study patient. (A) The ultrasound image of thyroid nodule preablation (hypoechoic nodule). (B) The vascularity of the nodule preablation. (C) Percutaneous RFA of the thyroid nodule (moving shot technique). (D) Ongoing RFA causing coagulative necrosis of the thyroid nodule represented as dense area (black arrow) along the needle track. (E) Completion of the RFA procedure (hyperechoic nodule). (F) Reduced vascularity of the nodule post-RFA procedure (in comparison to image B).

Abbreviations: RFA, radiofrequency ablation.

Our rate of success in resolving hyperthyroidism is superior to the published data on average (90.9% vs 67%) (Table 3). Furthermore, this was achieved expeditiously, in many cases within the first 3 to 6 months. Encouragingly, most of these patients (81.8%, n = 18/22) remained euthyroid throughout the follow-up (mean duration of 16.5 months). Two patients (9.1%) developed mild subclinical hypothyroidism requiring a small dose of levothyroxine supplementation therapy. The 2 patients described earlier with recurrent/residual hyperthyroidism were able to undergo effective therapy (lobectomy and repeat RFA, respectively) without any untoward events related to prior RFA therapy. Most of our patients received general anesthesia during the RFA procedure (Fig. 3). This could potentially explain our superior results (90.9% vs 67%) in achieving euthyroid status compared to the literature (Table 3). It has been shown that patient anxiety associated with RFA procedures when performed under local anesthesia could be stressful for the radiologists and the RFA team [2]. The use of general anesthesia mitigates the patient anxiety, provides proper positioning of the neck while avoiding movements during the procedure, and, more importantly renders adequate time for the interventional radiologists to ablate the nodules thoroughly, including the margins. With this approach, the average duration required for the RFA procedure for AFTN was only around 12.00 minutes in our center (literature data unavailable for comparison). We also note the excellent result reported with conscious sedation, which seems to be an equal alternative to general anesthesia from that perspective. While we acknowledge that most centers do not follow these anesthetic approaches but rather prefer local anesthesia, we think that management of anesthesia should be part of the discussion, in view of our common goal of achieving maximal success rates.

Fortunately, none of the patients developed any severe, long-term complications following the RFA. Two patients did experience transient palpitations, requiring short-term beta-blocker therapy (less than a week). This possibly relates to a sudden surge in circulating T4 hormone post-RFA. While these are transient events, we are currently exploring whether consistently normalizing thyroid levels before ablation (including in asymptomatic patients) and continuing ATD therapy for 1 week after ablation could eliminate them altogether. A retrospective study reviewing 875 patients who underwent RFA for recurrent thyroid cancers and benign thyroid nodule showed an overall complication rate of 3.5% (31/875), and 1.6% (14/875) had major complications, particularly higher when treating recurrent thyroid cancer [3]. An Austrian study using RFA for benign thyroid nodules for 277 patients described the overall complication rate at 16.8% with 3.2% moderate (reversible) and 0.7% long-term or severe (hypothyroidism and wound infection) [2]. A comparative study between RFA and surgery (n = 200 each) for benign thyroid nodule favored RFA, showing a 6% complication rate in patients who underwent surgery as opposed to 1% in the RFA group ($P < .002$) [14].

Though no formal assessment (questionnaire based) was employed, all patients were satisfied after going through RFA treatment, particularly regarding the normalization of thyroid function and thyrotoxic symptom improvement. In addition, the postprocedural SYS showed a significant improvement in local symptoms when present, on par with the literature data [3].

Both RAI treatment and surgery are effective therapies for AFTN and are considered the standard choices [10]. However, the risks of surgery and long-term hypothyroidism with its implications on overall health, in particular in women planning pregnancy, opens these choices for debate [18, 19]. Furthermore, some patients are concerned about radiation exposure in general, while others perceive a negative impact from a scar on the exposed neck, making these standard choices less desirable. Therefore, a number of professional societies (American Association of Clinical Endocrinology [26], Italian Working Group on Minimally Invasive Treatments of the Thyroid [11], European Thyroid Association [27], Korean Society of Thyroid Radiology [12]), have started to support RFA as a choice for AFTN [28], particularly when surgery and RAI are either contraindicated or declined by the patient. In 2018, the Korean Society of Thyroid Radiology outlined that RFA can be indicated for either toxic or pretoxic AFTN (weak recommendation, moderate quality evidence) [12]. In our cohort, almost all patients decided to undergo RFA due to personal choice, to avoid permanent hypothyroidism and any surgical complications.

Though there is paucity of data to demonstrate the long-term efficacy of RFA treatment for AFTNs, our cohort supports the efficacy of RFA as a promising alternative to surgery or RAI in resolving hyperthyroidism. For our 1 patient who proceeded to lobectomy for recurrent disease, it is likely that a repeat RFA session would have achieved final resolution of his AFTN. This raises the interesting question whether repeat RFA could also be endorsed for recurrent disease considering its low-risk profile [14].

There are several limitations to our study that also apply to most studies on RFA for AFTN. Most of these patients were carefully selected (based on imaging features and patients' therapeutic preferences) and have not been treated in a randomized controlled trial setting. We also acknowledge our small sample size. Early on, patient selection included several patients willing to accept self-pay if denied coverage by their insurance, but that became unnecessary for most of our patients. These aspects limit the generalizability of the findings to the overall population of AFTN patients. While more data accumulate, development of a predictive model to ascertain the efficacy of RFA treatment based on the patient and/or nodule characteristics may be helpful in choosing RFA for the right patient population.

Conclusion

At this point, the standard of care for toxic adenomas remains surgery and/or RAI. However, based on our findings and the presented literature, we have found RFA of AFTNs is highly effective and safe. We propose that RFA, performed at centers of excellence by experienced operators, could be an attractive and effective therapy for AFTNs with a high likelihood of resolving hyperthyroidism and avoiding long-term complications, particularly permanent hypothyroidism. We look forward to larger studies that will help to clarify the role of RFA in patients with AFTN.

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Author Contributions

M.S.: Conceptualization, Methodology, Reviewing and Editing. M.D.: Data curation, Writing-Original draft preparation. A.R.: Data curation. J. S.: Reviewing and Editing. M.R.C.: Reviewing and Editing. J.C.M. III: Reviewing and Editing. R.A.L.: Reviewing and Editing. D.H.: Data curation, Reviewing and Editing. M.R.C.: Reviewing and Editing.

Disclosures

The authors have no relevant disclosures.

Data Availability

Some or all datasets generated during and/or analyzed during the current study are not publicly available but are available from the corresponding author on reasonable request.

References

1. Magister MJ, Chaikhoutdinov I, Schaefer E, Williams N, Saunders B, Goldenberg D. Association of thyroid nodule size and Bethesda class with rate of malignant disease. *JAMA Otolaryngol Head Neck Surg*. 2015;141(12):1089-1095.
2. Dobnig H, Amrein K. Monopolar radiofrequency ablation of thyroid nodules: a prospective Austrian single-center study. *Thyroid*. 2018;28(4):472-480.
3. Kim C, Lee JH, Choi YJ, Kim WB, Sung TY, Baek JH. Complications encountered in ultrasonography-guided radiofrequency ablation of benign thyroid nodules and recurrent thyroid cancers. *Eur Radiol*. 2017;27(8):3128-3137.
4. Hodax JK, Reinert SE, Quintos JB. Autonomously functioning thyroid nodules in patients <21 years of age: the Rhode Island hospital experience from 2003-2013. *Endocr Pract*. 2016;22(3):328-337.
5. Niedziela M, Breborowicz D, Trejster E, Korman E. Hot nodules in children and adolescents in western Poland from 1996 to 2000: clinical analysis of 31 patients. *J Pediatr Endocrinol Metab*. 2002;15(6):823-830.
6. Corrias A, Mussa A, Baronio F, *et al*. Diagnostic features of thyroid nodules in pediatrics. *Arch Pediatr Adolesc Med*. 2010;164(8):714-719.
7. Corvilain BDJ, Vassart G. *Toxic Adenoma and Toxic Multinodular Goiter*. Lippincott Williams and Wilkins; 2000:9.
8. Gupta A, Ly S, Castroneves LA, *et al*. A standardized assessment of thyroid nodules in children confirms higher cancer prevalence than in adults. *J Clin Endocrinol Metab*. 2013;98(8):3238-3245.
9. Hussain I, Zulfiqar F, Li X, Ahmad S, Aljammal J. Safety and efficacy of radiofrequency ablation of thyroid nodules-expanding treatment options in the United States. *J Endocr Soc*. 2021;5(8):bvab110.
10. Bahn RS, Burch HB, Cooper DS, *et al*. Hyperthyroidism and other causes of thyrotoxicosis: management guidelines of the American Thyroid Association and American Association of Clinical Endocrinologists. *Thyroid*. 2011;21(6):593-646.
11. Garberoglio R, Aliberti C, Appetecchia M, *et al*. Radiofrequency ablation for thyroid nodules: which indications? The first Italian opinion statement. *J Ultrasound*. 2015;18(4):423-430.
12. Kim JH, Baek JH, Lim HK, *et al*. 2017 Thyroid radiofrequency ablation guideline: Korean Society of Thyroid Radiology. *Korean J Radiol*. 2018;19(4):632-655.

13. Hamidi O, Callstrom MR, Lee RA, *et al.* Outcomes of radiofrequency ablation therapy for large benign thyroid nodules: a mayo clinic case series. *Mayo Clin Proc*. 2018;93(8):1018-1025.
14. Che Y, Jin S, Shi C, *et al.* Treatment of benign thyroid nodules: comparison of surgery with radiofrequency ablation. *AJNR Am J Neuroradiol*. 2015;36(7):1321-1325.
15. Baek JH, Jeong HJ, Kim YS, Kwak MS, Lee D. Radiofrequency ablation for an autonomously functioning thyroid nodule. *Thyroid*. 2008;18(6):675-676.
16. Papini E, Bizzarri G, Bianchini A, *et al.* Percutaneous ultrasound-guided laser ablation is effective for treating selected nodal metastases in papillary thyroid cancer. *J Clin Endocrinol Metab*. 2013;98(1):E92-E97.
17. Shin JE, Baek JH, Lee JH. Radiofrequency and ethanol ablation for the treatment of recurrent thyroid cancers: current status and challenges. *Curr Opin Oncol*. 2013;25(1):14-19.
18. Sung JY, Baek JH, Jung SL, *et al.* Radiofrequency ablation for autonomously functioning thyroid nodules: a multicenter study. *Thyroid*. 2015;25(1):112-117.
19. Spiezia S, Garberoglio R, Milone F, *et al.* Thyroid nodules and related symptoms are stably controlled two years after radiofrequency thermal ablation. *Thyroid*. 2009;19(3):219-225.
20. Stan MN. Supplemenatary Material for "Outcomes of Radiofrequency Ablation for Autonomously Functioning Thyroid Adenomas—Mayo Clinic Experience". Methods descriptor [Dataset]. *Dryad*. 2024. Deposited October 28, 2024. https://doi.org/10.5061/dryad.j9kd51cnt
21. Zingrillo M, Collura D, Ghiggi MR, Nirchio V, Trischitta V. Treatment of large cold benign thyroid nodules not eligible for surgery with percutaneous ethanol injection. *J Clin Endocrinol Metab*. 1998;83(11):3905-3907.
22. Jeong WK, Baek JH, Rhim H, *et al.* Radiofrequency ablation of benign thyroid nodules: safety and imaging follow-up in 236 patients. *Eur Radiol*. 2008;18(6):1244-1250.
23. Navin PJ, Thompson SM, Kurup AN, *et al.* Radiofrequency ablation of benign and malignant thyroid nodules. *Radiographics*. 2022;42(6):1812-1828.
24. Mauri G, Pacella CM, Papini E, *et al.* Image-Guided thyroid ablation: proposal for standardization of terminology and reporting criteria. *Thyroid*. 2019;29(5):611-618.
25. Deandrea M, Limone P, Basso E, *et al.* US-guided percutaneous radiofrequency thermal ablation for the treatment of solid benign hyperfunctioning or compressive thyroid nodules. *Ultrasound Med Biol*. 2008;34(5):784-791.
26. Jasim S, Patel KN, Randolph G, *et al.* American association of clinical endocrinology disease state clinical review: the clinical utility of minimally invasive interventional procedures in the management of benign and malignant thyroid lesions. *Endocr Pract*. 2022;28(4):433-448.
27. Papini E, Monpeyssen H, Frasoldati A, Hegedus L. 2020 European thyroid association clinical practice guideline for the use of image-guided ablation in benign thyroid nodules. *Eur Thyroid J*. 2020;9(4):172-185.
28. Orloff LA, Noel JE, Stack BC, *et al.* Radiofrequency ablation and related ultrasound-guided ablation technologies for treatment of benign and malignant thyroid disease: an international multidisciplinary consensus statement of the American head and neck society endocrine surgery section with the Asia pacific society of thyroid surgery, associazione medici endocrinologi, British association of endocrine and thyroid surgeons, European thyroid association, Italian society of endocrine surgery units, Korean society of thyroid radiology, Latin American thyroid society, and thyroid nodules therapies association. *Head Neck*. 2022;44(3):633-660.