Radiology: Imaging Cancer

ORIGINAL RESEARCH

Safety and Efficacy of Thermal Ablation for Benign Thyroid Nodules in Patients with or without Previous Thyroid Surgery

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Purpose: To examine the use of propensity score matching (PSM) to compare the safety and efficacy of US-guided thermal ablation (TA) as a first-line treatment for initial thyroid nodules versus as a second-line treatment for recurrent nodules following thyroid surgery.

Materials and Methods: This retrospective study included data from 693 patients with benign thyroid nodules (BTNs) who underwent US-guided TA between January 2015 and July 2023. These included 619 patients in the initial nodule group and 74 patients in the recurrent nodule group. PSM was employed to balance preablation data and minimize confounding bias between the two groups. The perioperative and post-TA complication rates of the two matched patient groups were compared. Nodule volume and volume reduction rate (VRR) were compared at 1, 3, 6, and 12 months after TA. Thyroid function, symptoms, and cosmetic scores were also compared.

Results: Successful matching of 222 patients (mean age ± SD, 55.92 years ± 12.08; 172 female) (2:1 ratio) was achieved, with 148 patients in the initial nodule group and 74 patients in the recurrent nodule group. There was no evidence of a difference between the two groups regarding incidence of major complications ($P > .99$), minor complications ($P = .82$), or adverse effects ($P = .51$). The difference in VRR between the two groups at each follow-up point was not statistically significant ($P = .30, .28, .33, .20, .33$, respectively). At the last follow-up, symptom and cosmetic scores were significantly reduced in both groups (both $P < .01$), whereas serum thyroid hormone levels were not significantly different from those before TA treatment (all $P > .05$).

Conclusion: US-guided TA treatment exhibited a favorable safety and efficacy profile for patients with BTNs, regardless of prior thyroid surgery.

Supplemental material is available for this article.

Thyroid nodules (TN) have become a prevalent clinical issue, seen in 20%–70% of individuals (1,2). Guidelines recommend surgery as the first-line treatment for thyroid cancer and benign TNs (BTNs) causing compression symptoms or cosmetic problems (3). Within 40 years after the initial lobectomy, up to 20%–59% of patients may develop another nodule with symptoms, malignant recurrence, or local neoplastic lesions (4). Surgery is the standard treatment for patients with local recurrence. However, repeat surgery poses a significant challenge for surgeons due to the distortion, fibrosis, and adhesions of normal anatomic neck tissues after initial thyroid surgery, thereby increasing the risk of complications (such as permanent recurrent laryngeal nerve paralysis and hypoparathyroidism) following repeat surgery (5). Increased adverse effects of lifelong thyroid hormone supplementation on the patient's skeletal and cardiovascular systems after repeat surgery, along with unsatisfactory cosmetic outcomes, can reduce the patient's health-related quality of life. Consequently, this may potentially discourage patients from considering repeat surgery for recurrent nodules (2,3,6,7). The American Thyroid Association guidelines underscore the imperative of "minimizing treatment-related morbidity and avoiding unnecessary interventions" (3), necessitating physicians and patients to comprehensively evaluate the risks and benefits associated with diverse treatment alternatives when making informed decisions. Therefore, exploring appropriate treatment strategies is crucial to improve prognosis of patients with recurrent nodules who have undergone thyroid surgery.

In recent years, minimally invasive image-guided thermal ablation (TA) techniques such as percutaneous microwave ablation (MWA) and radiofrequency ablation (RFA) have been proven in clinical practice and recommended as safe and effective alternative treatment options to surgery for thyroid diseases (8–12). TA therapy is also an effective treatment option for patients with recurrent BTNs and thyroid cancer who decline repeat surgery or are deemed high-risk candidates for another surgery (3,13–15). However, limited studies have reported the efficacy of RFA in patients with recurrent BTNs who have undergone prior lobectomy, with volume reduction rates (VRRs) of up to 81.2%–87.2% (16–18). To date, few studies have reported complication rates following TA for recurrent TNs. In addition, we found no comparative studies on the complications and efficacy of TA techniques in the treatment of initial nodules and recurrent nodules after previous surgery. Therefore, the aim of this study was to compare the complication rates and efficacy of US-guided TA as a first-line treatment for initial nodules and as a second-line treatment for recurrent nodules after previous thyroid surgery.

Materials and Methods

This retrospective cohort study was approved by the institutional ethical review committee of our hospital (SHSY-IEC-4.1/21–366/01). After full explanation of the nature of invasive procedures, each patient provided written consent before undergoing US-guided fine-needle aspiration cytology or TA.

Abbreviations

BTN = benign thyroid nodule, MWA = microwave ablation, PSM = propensity score matching, TA = thermal ablation, TN = thyroid nodule, RFA = radiofrequency ablation, VRR = volume reduction rate

Summary

US-guided thermal ablation was feasible in patients with recurrent benign thyroid nodules, demonstrating safety and efficacy profiles comparable to those in patients with initial benign thyroid nodules.

Key Points

- There was no evidence of a difference in complication rates and treatment efficacy after thermal ablation (TA) treatment in patients with initial versus recurrent benign thyroid nodules (all $P > .05$).
- Thyroid function remained stable in the recurrent nodule group after TA treatment (both $P > .05$).
- At the last follow-up, both groups achieved great volume reduction rates (87.8% ± 16.4 vs 86.5% ± 18.7; $P = .33$), with significant improvement in patient symptoms and cosmetic scores (all $P > .05$).

Keywords

Head/Neck, Thyroid, Treatment Effects, Efficacy Studies, Ablation Techniques (Radiofrequency, Thermal, Chemical)

Patients

Between January 2015 and July 2023, a total of 1064 patients received US-guided TA for BTNs at our center. Among them, 963 patients received TA as first-line treatment for initial TNs. Another 101 patients who had undergone thyroid surgery received TA as second-line treatment for recurrent TNs. Among these 117 patients with recurrent TNs, some refused another operation due to a fear of surgical complications, whereas others were deemed high-risk candidates who could not tolerate repeat surgery and ultimately opted for TA therapy. All enrolled patients met the following inclusion criteria: *(a)* benign diagnosis confirmed twice with fine-needle aspiration cytology; *(b)* received a single session of RFA or MWA treatment; *(c)* follow-up exceeding 6 months; and *(d)* normal hepatic and renal function and coagulation parameters. Exclusion criteria included *(a)* malignant nodules confirmed with fine-needle aspiration cytology; *(b)* incomplete clinical or imaging data; *(c)* coagulation disorders or severe organ failure; and *(d)* patients scheduled to receive staged RFA or MWA therapy. The study flowchart is shown in Figure 1.

Preoperative Evaluation

All patients underwent routine US, US-guided fine-needle aspiration cytology, and laboratory tests before TA. The position, largest diameter, and US characteristics of the nodule were assessed using conventional US. Nodule volume follows the following equation: $V = \pi \times abc \div 6$ (where V is the volume, a is the maximum diameter, b and c are the other two vertical diameters) (19). The VRR was employed to assess the ablation efficacy and was computed as follows: VRR = ([initial volume – final volume] × 100%) ÷ initial volume (20). Recurrent nodules were defined as new lesions in the remaining thyroid tissue detected with US after previous surgery (21). Laboratory tests included complete blood counts, coagulation function tests, and thyroid function tests (ie, free triiodothyronine, free thyroxine, and thyroid-stimulating hormone [TSH]). Patients receiving anticoagulant medications were required to discontinue them for 1 week before treatment.

Each patient self-scored symptoms associated with dysphagia and neck compression using a 10-cm visual analog scale ranging

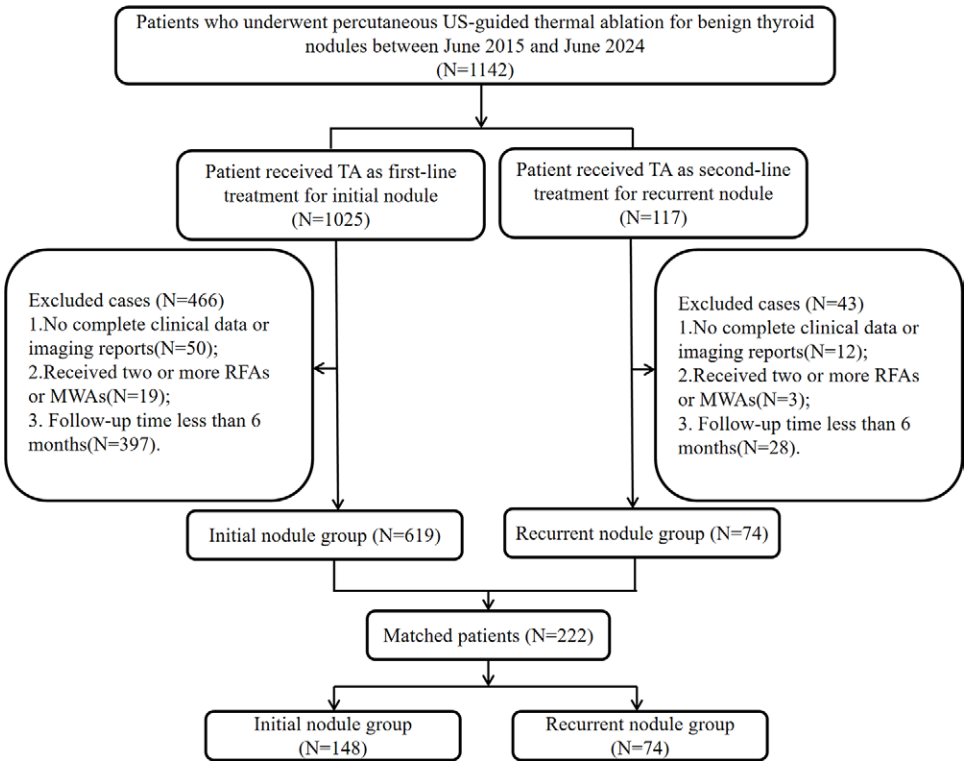

Figure 1: Flowchart of patient inclusion in both groups. MWA = microwave ablation, RFA = radiofrequency ablation, TA = thermal ablation.

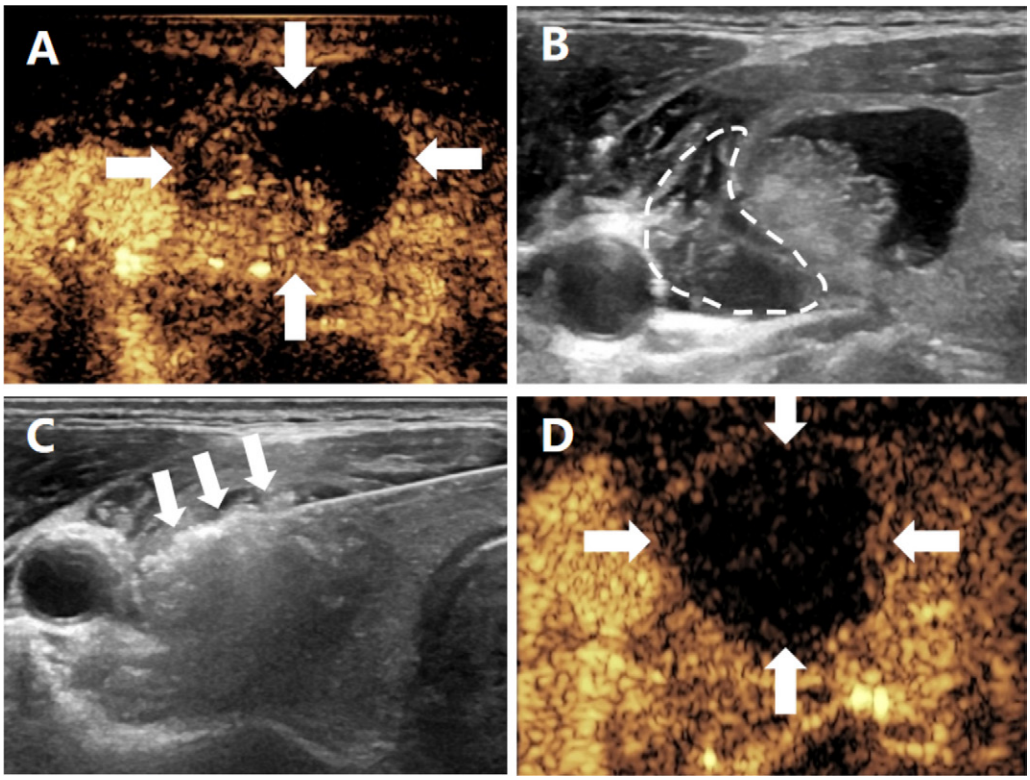

Figure 2: US images in a 47-year-old woman with a benign thyroid nodule in the right lobe of the thyroid gland who underwent microwave ablation. **(A)** Contrast-enhanced image of the nodule (arrows) before ablation. **(B)** Image after injection of a mixture of 0.9% saline and lidocaine to isolate the thyroid gland from surrounding critical structures (the outline of the white curve shows the resulting water-isolated area). **(C)** Image shows the hypoechoic zone produced by the ablation needle within the nodule during ablation (arrows). **(D)** Postablation contrast-enhanced image shows no contrast agent perfusion within the nodule (arrows).

from 1 (no symptoms) to 4 (worst symptoms). The physician evaluated cosmetic scores as follows: 1, no palpable mass; 2, no cosmetic problem but a palpable mass; 3, cosmetic problem occurring only with swallowing; and 4, easily detectable cosmetic problem (13).

Ablation Procedures

All ablation procedures were performed by certified operators with at least 5 years of interventional US experience using the same ablation devices. Ablation devices include MWA instrument (KY-2000; Kangyou Medical) and RFA instrument (STARmed; Celon AG Medical). The selection of ablation technique was based on the patient's condition and the doctor's recommendation.

TA procedure was performed in the operating room. The patient was placed in a supine position with the neck extended. Before TA, the operator carefully evaluated the relationship between the nodules and critical structures (such as vessels, esophagus, and trachea) using high spatial resolution US to determine the optimal puncture path. Sterilization and local anesthesia administration of 2% lidocaine were then carried out. This was followed by injecting a mixture of 0.9% normal saline and lidocaine into the area surrounding the thyroid capsule (≥0.5 cm between the capsule and neighboring critical structures) for the hydrodissection technique, forming a safety barrier against thermal damage to critical structures (13,22). At the beginning of TA, the electrode tip should be positioned at the deepest and farthest point within the nodule under real-time US guidance, subsequently advancing from deep to shallow layer by layer until complete ablation of the entire nodule is achieved. This approach is also known as the moving shot technique (23). The initial power during ablation was set at 20–35 W for MWA and 20–30 W for RFA, following which the power was gradually increased until a transient hyperechoic zone appeared at the electrode tip. In case of intolerable pain reported by the patient during TA, power reduction or temporary pause in ablation should be considered for a few seconds. The ablation procedure was terminated when the entire nodule was completely covered by the transient hyperechoic zone (24).

Contrast-enhanced US was performed 3–5 minutes later. If the ablated area showed no enhancement, complete ablation was achieved. If the ablated area showed residual enhancement as the contrast agent (SonoVueR, 2.4 mL; SonoVue) entered, it was considered incomplete ablation and required immediate supplementary ablation (25). The step-by-step illustrations of the MWA and RFA techniques are shown in Figure 2 and Figure 3, respectively. After the TA procedure, all patients were carefully observed for half an hour, and ablation-related complications were recorded in detail.

Postablation Assessment and Follow-up

Data collected included demographic characteristics, nodule characteristics, symptom and cosmetic scores, thyroid function, complications, and adverse effects. US evaluation was conducted at 1, 3, 6, and 12 months after TA and every 12 months thereafter, followed by thyroid function monitoring and collection of patients' symptom and cosmetic scores. Contrast-enhanced US

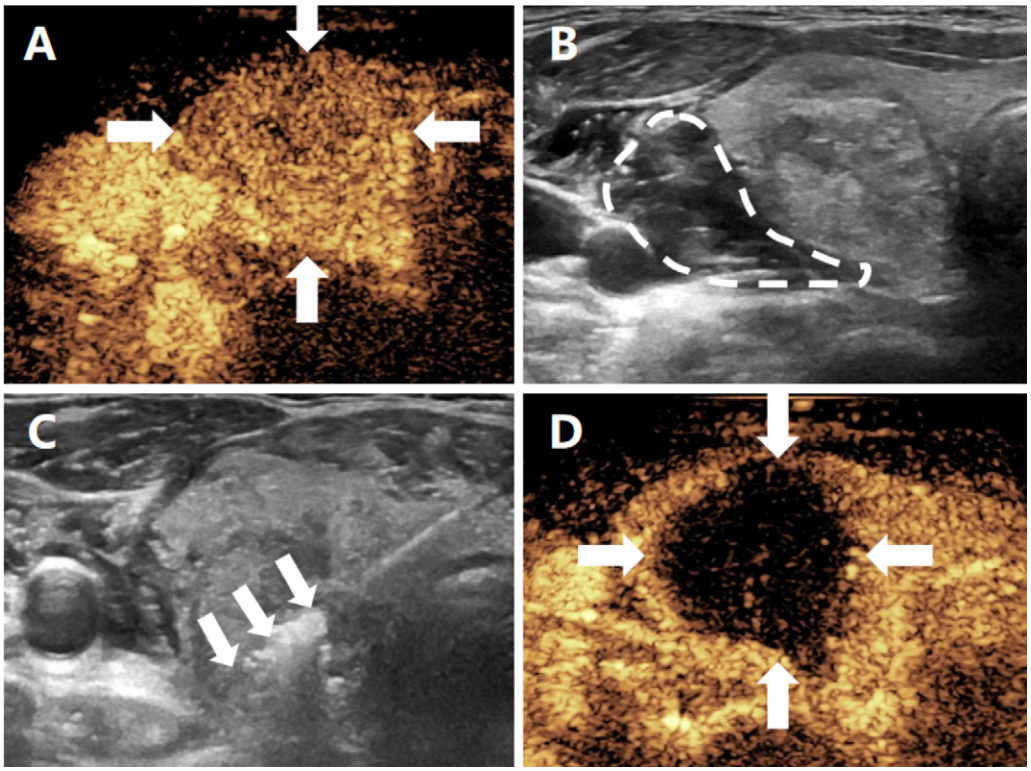

Figure 3: US images in a 47-year-old woman with a benign thyroid nodule in the right lobe of the thyroid gland who underwent radiofrequency ablation. **(A)** Contrast-enhanced image of the nodule (arrows) before ablation. **(B)** Image after injection of a mixture of 0.9% saline and lidocaine to isolate the thyroid gland from surrounding critical structures (the outline of the white curve shows the resulting water-isolated area). **(C)** Images shows the hypoechoic zone produced by the electrode tip within the nodule during ablation (arrows). **(D)** Postablation contrast-enhanced image shows no contrast agent perfusion within the nodule (arrows).

was performed to assess the efficacy of local thermal ablation at the 1-month follow-up. During follow-up, a VRR above 50% was considered therapeutic success (19,26). Regrowth was defined as the appearance of new blood flow within the nodule in the ablation zone and/or an increase in volume exceeding 50% compared with previous measurements (3,20).

Definition of Complications and Adverse Effects

Major and minor complications as well as adverse effects during the perioperative and follow-up periods were evaluated with reference to the Society of Interventional Radiology (27,28). Major complications are defined as those causing severe morbidity and disability events requiring hospitalization, or prolonged hospitalization and are life-threatening if not treated promptly. All other complications are considered minor complications. Adverse effects are defined as adverse consequences that do not necessitate treatment or prescription medications and seldom result in long-term clinical sequelae.

Statistical Analysis

The primary end point of this study was the incidence of complications. Secondary end points included reduction in nodule volume, VRR, improvement in symptom and cosmetic scores, and thyroid function. To minimize confounding bias, propensity score matching (PSM) was employed to overcome baseline covariate bias between the two groups (29,30). Baseline covariates included sex, age, number of treated nodules, nodule composition, position, volume, ablation mode, follow-up time, and symptom and cosmetic scores. The nearest neighbor method was used to match 619 patients with initial nodules with 74 patients with recurrent nodules (for a ratio of 2:1). After PSM, a total of 148 patients with initial nodules along with 74 patients with recurrent nodules were eventually enrolled. Qualitative variables are expressed as numbers and percentages of patients or nodules and analyzed using the χ^2 test or Fisher test. Quantitative variables are expressed as means and SDs and analyzed with the independent samples *t* test. Univariable and multivariable linear regression analyses were used to identify potential influences associated with VRR. Subgroup analyses were also performed to identify potential factors that may influence treatment effectiveness. Mixed-effects analysis was used to compare the change in VRR over time between the initial nodule group and the recurrent nodule group. All statistical analyses were performed using SPSS software (version 26.0; SPSS) and R (version 4.3.0; R Foundation for Statistical Computing). Significance level was defined as $P < .05$.

Results

Baseline Patient Characteristics

Baseline demographic and clinical data are summarized in Table 1. From January 2015 to June 2024, 1142 patients with BTNs underwent US-guided TA at our center, of whom 509 were excluded. The final study cohort consisted of 693 patients (mean age ± SD, 51.10 years ± 13.35; age range, 14–86 years) with 975 nodules. Patients were categorized into two groups

Table 1: Characteristics of Patients with Initial and Recurrent Thyroid Nodules

Characteristic	Before PSM			After PSM		
	Initial Nodule Group (n = 619)	Recurrent Nodule Group (n = 74)	P Value	Initial Nodule Group (n = 148)	Recurrent Nodule Group (n = 74)	P Value
Sex			.91			.57
Female	490 (79.2)	59 (79.7)		113 (76.4)	59 (79.7)	
Male	129 (20.8)	15 (20.3)		35 (23.6)	15 (20.3)	
Age (y)	50.54 ± 13.35	55.72 ± 12.54	.002*	55.17 ± 13.09	56.16 ± 12.52	.62
Composition			.37			
Predominantly cystic	208 (33.6)	28 (37.8)		64 (43.2)	28 (37.8)	
Predominantly solid	145 (23.4)	12 (16.2)		26 (17.6)	12 (16.2)	
Solid	266 (43.0)	34 (45.9)		58 (39.2)	34 (45.9)	
No. of treated nodules			.45			.85
1	404 (65.3)	45 (60.8)		92 (62.2)	45 (60.8)	
>1	215 (34.7)	29 (39.2)		56 (37.8)	29 (39.2)	
Position			.04*			.98
Right lobe	310 (50.1)	34 (44.6)		67 (43.9)	33 (44.6)	
Left lobe	284 (45.9)	33 (45.9)		70 (47.3)	34 (45.9)	
Isthmus	25 (4.0)	7 (9.5)		13 (8.8)	7 (9.5)	
Volume (mL)	8.32 ± 10.97	8.74 ± 8.10	.18	9.34 ± 10.29	8.74 ± 8.10	.78
Ablation mode			.29			>.99
RFA	126 (20.3)	19 (25.7)		38 (25.7)	19 (25.7)	
MWA	493 (79.6)	55 (74.3)		110 (74.3)	55 (74.3)	
Symptom score	2.47 ± 2.01	3.14 ± 1.87	.001*	3.25 ± 1.92	3.14 ± 1.87	.81
Cosmetic score	2.14 ± 1.16	1.96 ± 1.04	.29	2.05 ± 1.08	1.96 ± 1.04	.61
Follow-up time (mo)	15.50 ± 10.00	15.88 ± 13.85	.13	16.61 ± 11.15	15.88 ± 13.85	.09

Note.—Except where indicated, data are numbers of patients with percentages in parentheses or means ± SDs. MWA = microwave ablation, PSM = propensity score matching, RFA = radiofrequency ablation.
* $P < .05$ are statistically significant.

based on prior thyroid surgery: initial nodule group (n = 619) and recurrent nodule group (n = 74) (Fig 1). Due to unavoidable selection bias, patients in the recurrent nodule group were older than those in the initial nodule group, with statistically significant differences observed in symptom score and nodule position (Table 1). After performing PSM using the nearest neighbor method with a ratio of 2:1, a total of 222 patients were matched, comprising 148 patients with initial nodules and 74 patients with recurrent nodules. The initial nodule group included 113 female (mean age, 54.63 years ± 12.28) and 35 male (mean age, 60.40 years ± 9.27) patients, and the recurrent nodule group included 59 female (mean age, 55.73 years ± 11.88) and 15 male (mean age, 55.67 years ± 15.35) patients. After PSM analysis, no significant differences were observed in the baseline characteristics between the two groups.

Complications and Adverse Effects

As shown in Figure 4, we found no evidence of a statistically significant difference in the rates of complications and adverse effects between the initial nodule group and the recurrent nodule group (Table 2) (all $P > .05$). All patients tolerated the TA treatment well, with no serious life-threatening complications.

Major Complications

We found no evidence of a difference in the incidence of major complications between the two groups (0.7% vs 1.4%; $P > .99$). A total of two major complications were reported in this study, both presenting as transient hoarseness (Table 2). One case occurred in the initial nodule group and one case in the recurrent nodule group with prior thyroid surgery; however, all symptoms resolved within 2 and 3 months, respectively.

Minor Complications

The incidence of minor complications was 4.7% (seven of 148; 95% CI: 2.0, 10.0) in the initial nodule group and 4.1% (three of 74; 95% CI: 0.9, 11.9) in the recurrent nodule group with prior thyroid surgery (Table 2). No evidence of a significant difference was observed between the two groups ($P = .82$).

Two patients in the initial and one patient in the recurrent nodule group complained of neck swelling and tenderness half an hour after TA. Bedside US revealed perithyroidal and intrathyroidal hematomas, respectively. We attribute these hematomas to mechanical electrode injury or thyroidal vasodilation–induced hemorrhage. These hematomas can cause neck pressure or even dyspnea and demand immediate attention upon detection. After

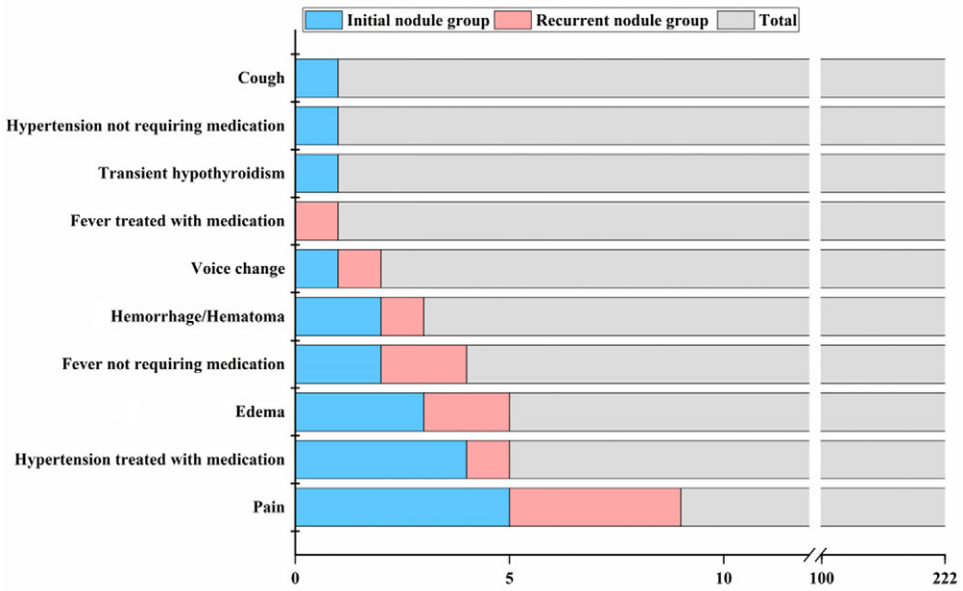

Figure 4: Bar charts show the number of patients with complications and adverse effects after thermal ablation in initial and recurrent nodule groups.

Table 2: Comparison of Complications and Adverse Effects in Patients in the Initial Nodule Group versus the Recurrent Nodule Group after TA

Complication or Adverse Effect	Initial Nodule Group (n = 148)	Recurrent Nodule Group (n = 74)	P Value
Major complications	1 (0.7)	1 (1.4)	>.99
Voice change	1 (0.7)	1 (1.4)	>.99
Minor complications	7 (4.7)	3 (4.1)	.82
Hemorrhage/hematoma	2 (1.4)	1 (1.4)	>.99
Fever treated with medication	0 (0)	1 (1.4)	.33
Transient hypothyroidism	1 (0.7)	0 (0)	>.99
Hypertension treated with medication	4 (2.7)	1 (1.4)	.50
Adverse effects	12 (8.1)	8 (10.8)	.51
Pain	5 (3.4)	4 (5.4)	.48
Edema	3 (2.0)	2 (2.7)	.75
Hypertension observed without medication	1 (0.7)	0 (0)	>.99
Fever not treated with medication	2 (1.4)	2 (2.7)	.49
Coughing	1 (0.7)	0 (0)	>.99

Note.—Except where indicated, data are numbers of patients with percentages in parentheses. Categorical variables were compared using the χ^2 test or Fisher exact test.

1 hour of hemostatic medication and/or mild neck compression, all hematomas absorbed and disappeared completely at 1 month follow-up after ablation.

Hypothyroidism occurred in one patient in the initial nodule group 1 month after ablation. It manifested as an increase (14.820 mU/mL) in serum thyroid-stimulating hormone concentration compared with the preablation period (0.650 mU/mL) but gradually decreased thereafter. At the 3-month follow-up, the thyroid-stimulating hormone concentration had returned to normal at 0.386 mU/mL (normal range: 0.38–4.34 mU/mL). Therefore, this hypothyroidism was considered transient.

Four patients in the initial nodule group and one patient in the recurrent nodule group exhibited a 20–30 mm Hg elevation in blood pressure during TA, which subsequently normalized following sublingual administration of nifedipine. These patients all had a history of underlying hypertension. We believe that raised blood pressure may be attributed to the release of thyroid hormones or pain during the TA procedure (31).

One patient in the recurrent nodule group experienced postoperative fever (temperature over 38 °C), which returned to normal the next day after taking antipyretic medication following the ineffective physical hypothermia with ice pack.

Adverse Effects

Twenty adverse effects were reported, including mild pain (n = 9), edema (n = 5), hypertension treated without medication (n = 1), mild fever untreated with medication (n = 4), and coughing (n = 1) (Table 2). Of these, 8.1% (12 of 148 patients; 95% CI:

Table 3: Change in Volume, Largest Diameter, and VRR of Benign Nodules Before Ablation and at Follow-up

	Initial Nodule Group (n = 218)			Recurrent Nodule Group (n = 113)			P Value		
Time Period	Volume (mL)	Diameter (cm)	VRR (%)	Volume (mL)	Diameter (cm)	VRR (%)	Volume	Diameter	VRR
Baseline	7.03 ± 9.23	2.53 ± 1.11	–	6.43 ± 7.47	2.50 ± 1.22	–	–	–	–
1 month	3.49 ± 4.88*	2.05 ± 0.85*	34.88 ± 45.53	2.99 ± 3.46*	1.95 ± 0.82*	35.24 ± 41.39	.35	.32	.30
3 months	1.87 ± 3.08*	1.60 ± 0.76*	61.48 ± 31.01	1.79 ± 2.22*	1.59 ± 0.85*	62.34 ± 42.37	.82	.84	.29
6 months	1.32 ± 2.43*	1.31 ± 0.83*	79.00 ± 26.74	1.02 ± 1.52*	1.23 ± 0.75*	75.60 ± 32.65	.22	.37	.33
12 months	0.80 ± 1.51*	1.01 ± 0.82*	86.68 ± 17.25	0.86 ± 1.70*	0.99 ± 0.82*	85.18 ± 19.92	.83	.93	.20
Last follow-up	0.93 ± 1.80*	1.02 ± 0.89*	87.80 ± 16.43	0.79 ± 1.22*	1.02 ± 0.81*	86.53 ± 18.73	.44	.96	.33

Note.—Data are means ± SDs. Comparisons between the two groups were made using the independent samples t test. VRR = volume reduction rate.
* Statistically significant.

4.6, 14.9) were in the initial nodule group and 10.8% (eight of 74; 95% CI: 5.4, 22.5) in the recurrent nodule group with previous thyroid surgery, with no significant difference between the two groups (P = .51).

The most common complaint was mild pain, mainly manifested by varying degrees of cervical pain during or following the TA procedure and occasionally radiating to the head and ears. However, this pain was mostly not persistent and could eventually be relieved. In four patients, pain was relieved by reducing or suspending electrode output for a few moments during the procedure, and no patient terminated the ablation prematurely due to pain. Three other patients experienced pain relief after applying ice packs for half an hour after TA. Only one patient took oral analgesics and achieved complete pain relief within 1 week.

One patient in each group experienced postablation edema (2.0%, three of 148 vs 2.7%, two of 74; P = .75), which was alleviated by applying ice packs for 2 hours without further treatment. Two patients each (1.4%, two of 148 vs 2.7%, two of 74; P =.49) developed mild fever after TA, and their temperatures returned to normal after 1 hour of physical cooling.

One patient in the initial nodule group exhibited elevated blood pressure during the TA procedure, despite having no history of hypertension. This increase was attributed to the patient's feeling of nervousness. The blood pressure returned to normal levels after suspending ablation and resting for half an hour, subsequently enabling the successful completion of the TA process.

One patient in the initial nodule group developed a transient cough lasting approximately 10–20 seconds during the TA procedure, likely attributed to tracheal heat propagation, and the cough was relieved immediately upon pausing the TA. No complications related to tracheal heat injury were observed during postoperative follow-up.

Treatment Efficacy

The mean follow-up duration was 16.61 months ± 11.15 in the initial nodule group, and 15.88 months ± 13.85 in the recurrent nodule group. The secondary end points of the treatment outcomes of nodules in both groups are shown in Table 3. Regarding the 218 nodules in the initial nodule group, the mean volume of the nodules decreased significantly from 7.03 mL ± 9.23 to 0.93 mL ± 1.80, with a VRR of 87.8% ± 16.4 (95% CI: 85.6, 90.0) at the last follow-up. For the 113 nodules in the recurrent nodule group, the mean volume of modules decreased significantly from 6.43 mL ± 7.47 to 0.79 mL ± 1.22 (both groups, P < .01). The VRR at the last follow-up was 86.5% ± 18.7 (95% CI: 83.0, 90.0) (Fig 5A–5C). No evidence of 6-month VRR difference was observed between MWA and RFA for BTNs (P = .63). There were no significant differences in volume, largest diameter, and VRR between the two groups at each follow-up time point (all P > .05) (Table 3). Mixed-effects analysis showed no evidence of a difference in the change in VRR over time between the two groups (β coefficient = 0.1%; 95% CI: −0.28, 0.56; P = .52) (Table S1). At the last follow-up, a total of 95.8% (317 of 331) nodules achieved therapeutic success, and 26.3% (87 of 331) nodules were completely absorbed. No regrowth was observed in this study. Figure 6 demonstrates the ideal treatment progression.

At the last follow-up, symptom and cosmetic scores of patients in the initial nodule group decreased significantly from 3.25 ± 1.92 to 0.22 ± 0.49 and from 2.05 ± 1.08 to 1.01 ± 0.12 (both P < .001). There were significant reductions in the recurrent nodule group from 3.14 ± 1.87 to 0.26 ± 0.47 and from 1.96 ± 1.04 to 1.01 ± 0.12 (both P < .001) (Table 4). We found no evidence of a significant difference between the two groups (Figs 5D, 5E). Thyroid function of patients in the initial nodule group remained stable following TA, as demonstrated by insignificant changes in mean serum free triiodothyronine, free thyronine, and thyroid-stimulating hormone levels at the last follow-up compared with baseline levels (both P > .05) (Table 4). The same held true for patients in the recurrent nodule group because their thyroid function remained unaffected by TA treatment. Furthermore, those who were already taking thyroid hormone supplements before TA did not require an escalation in therapeutic dosage after TA.

Univariable, Multivariable, and Subgroup Analyses

Univariable and multivariable analyses demonstrated that nodule composition (β coefficient = −0.18; 95% CI: −0.26, 0.10; P < .001) was an independent factor associated with VRR (Table S2). Nevertheless, when patients were divided into different subgroups based on these variables, no differences were observed in VRR among the different subgroups (Fig 7).

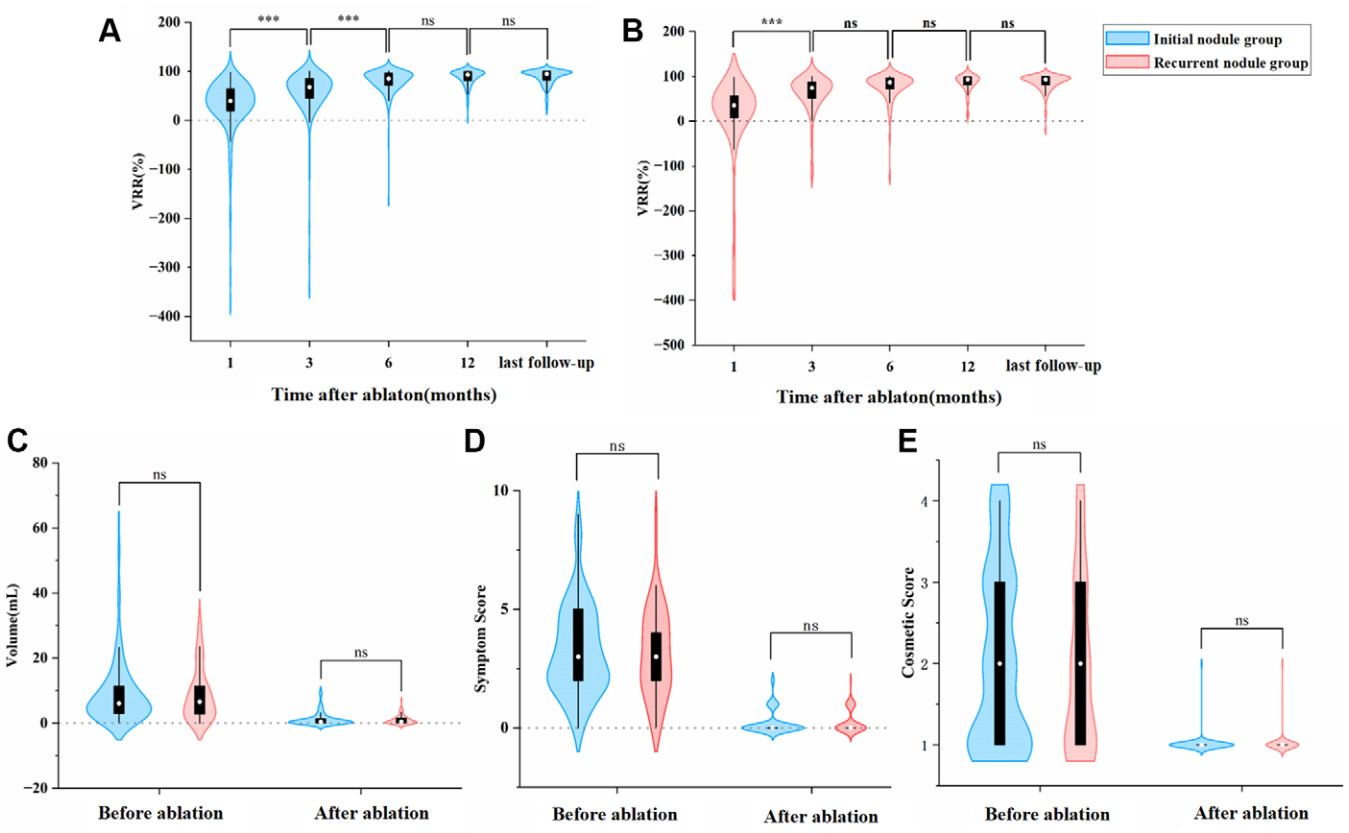

Figure 5: **(A, B)** Violin plots show the change in volume reduction rate (VRR) over time between the initial nodule group **(A)** and the recurrent nodule group **(B)**. **(C-E)** Violin plots show that no significant differences were found between the two groups in nodule volume **(C)**, symptom score **(D)**, and cosmetic score **(E)** before ablation and at the last follow-up after ablation. The top and bottom edges of the box represent the third quartile and the first quartile, respectively. The box's height is the IQR, showing the spread of the middle 50% of data. A small square inside the box indicates the median, reflecting central tendency. The dashed lines mark a zero value to compare data against the standard. ns = no significance.

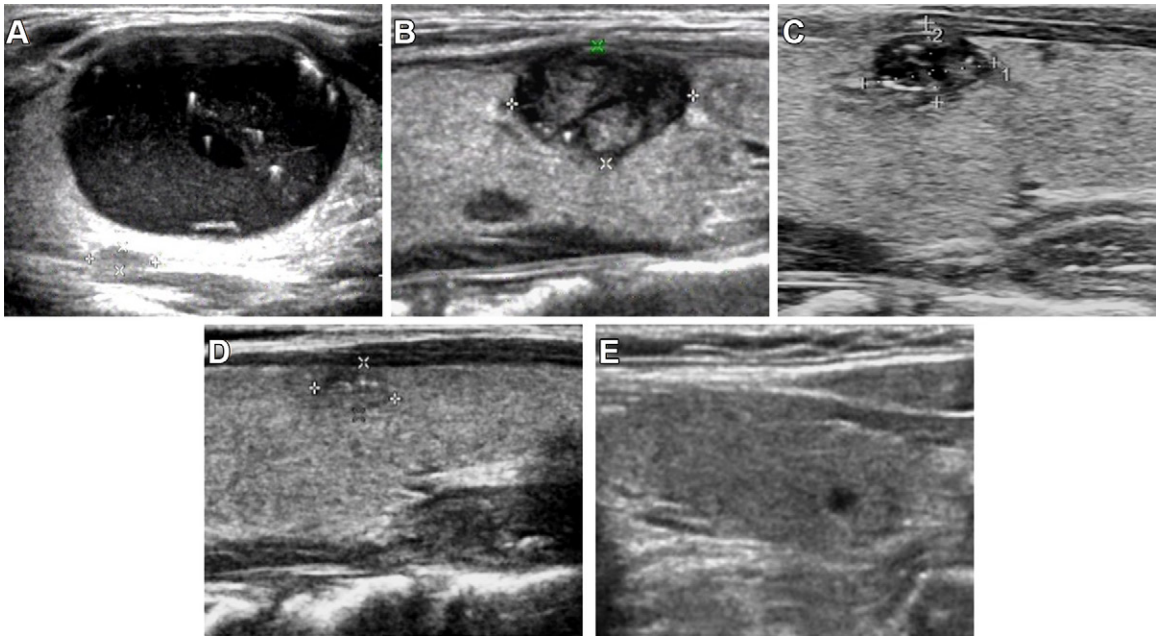

Figure 6: Grayscale US images of treatment progress in a 50-year-old woman who underwent microwave ablation for a predominantly cystic nodule in the right lobe of the thyroid gland. **(A)** The nodule before ablation treatment; its volume was 12.36 mL. **(B)** At the 1-month follow-up after treatment, the nodule volume was reduced to 0.92 mL with a volume reduction rate (VRR) of 92.58%. **(C)** At the 3-month follow-up after treatment, the nodule volume was reduced to 0.12 mL with a VRR of 99.05%. **(D)** At the 6-month follow-up after treatment, the nodule volume was reduced to 0.06 mL with a VRR of 99.53%. **(E)** US image of the nodule at the 12-month follow-up after treatment; the nodule was completely absorbed with 100% VRR.

Table 4: Changes in Thyroid Function and Symptom and Cosmetic Scores Before and After TA

	Initial Nodule Group (n = 148)			Recurrent Nodule Group (n = 74)		
Parameter	Baseline	Last Follow-up	P Value	Baseline	Last Follow-up	P Value
FT3, pmol/L*	4.80 ± 1.41	4.74 ± 0.82	.58	4.73 ± 0.98	4.74 ± 0.81	.90
FT4, pmol/L†	15.85 ± 2.69	16.12 ± 2.28	.32	16.54 ± 3.19	16.19 ± 3.01	.41
TSH, mU/L‡	1.84 ± 0.98	2.04 ± 1.01	.07	1.87 ± 1.25	1.94 ± 1.18	.69
Symptom score	3.25 ± 1.92	0.22 ± 0.49	<.001§	3.14 ± 1.87	0.26 ± 0.47	<.001§
Cosmetic score	2.05 ± 1.08	1.01 ± 0.12	<.001§	1.96 ± 1.04	1.01 ± 0.12	<.001§

Note.—Except where indicated, data are means ± SDs. FT3 = free triiodothyronine, FT4 = free thyroxine, TA = thermal ablation, TSH = thyroid-stimulating hormone. P values are within-group comparisons of the initial levels of the corresponding indicators with those at the last follow-up after thermal ablation in both groups.
* Normal range: 2.80–6.30 pmol/L.
† Normal range: 10.50–24.40 pmol/L.
‡ Normal range: 0.38–4.34 mU/L.
§ Statistically significant.

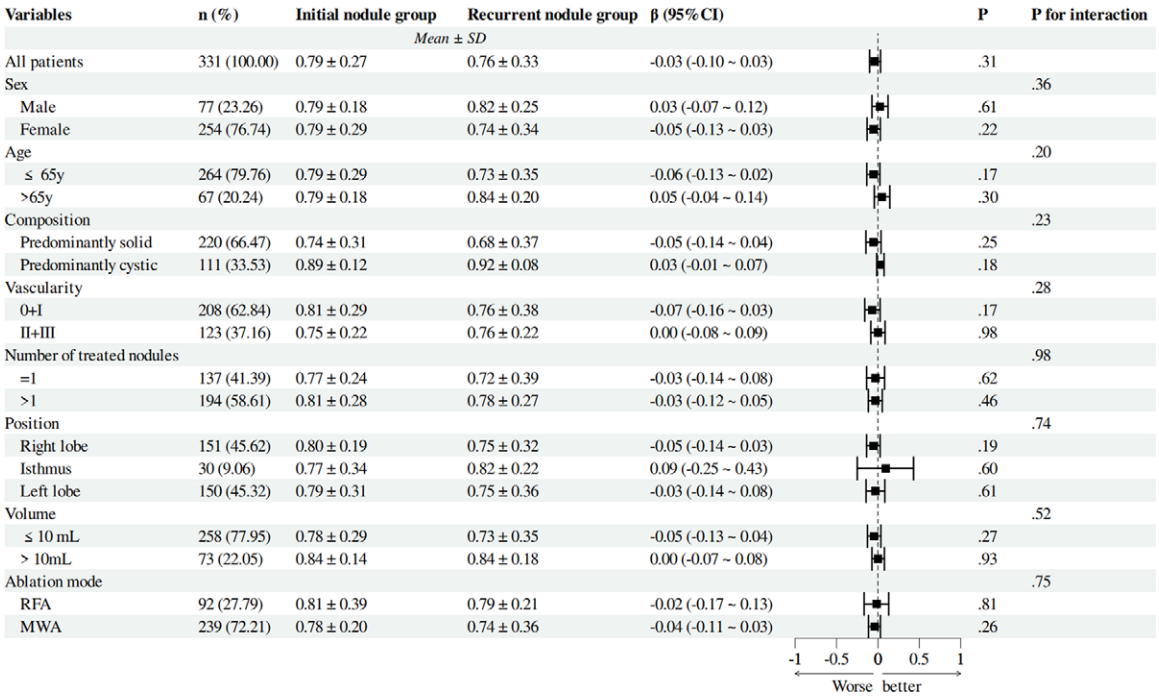

Figure 7: Forest plot of subgroup analysis of VRR (including sex, age, composition, vascularity, number of treated nodules, position, volume, ablation mode) at 6-month follow-up. MWA = microwave ablation, RFA = radiofrequency ablation, VRR = volume reduction rate.

Discussion

We successfully compared the complication rate and efficacy of TA therapy in patients with initial thyroid nodules and recurrent nodules by PSM. The results confirmed that there was no significant difference in the complication rate between the two groups (all P > .05). At the last follow-up, comparable VRRs were achieved for nodules in both groups (87.8% ± 16.4 vs 86.5% ± 18.7, P = .33). The patients' symptoms and cosmetic scores have also improved significantly (both P < .001). More importantly, thyroid function remained stable in both groups (all P > .05).

In this study, we determined that the mean VRR of the initial nodule group at the last follow-up was 87.8% ± 16.4, whereas the mean VRR of the recurrent nodule group was 86.53% ± 18.73, with no significant difference between the two groups (P > .05). There was also no evidence of observed changes in VRR over time between the two groups (P = .52). In addition, 95.41% (208 of 218) of nodules in the initial nodule group achieved therapeutic success, and 27.06% (59 of 218) of nodules were completely absorbed. In the recurrent nodule group, 96.46% (109 of 113) and 24.78% (28 of 113) of nodules achieved therapeutic success and completely absorbed, respectively. There was no statistically significant difference in therapeutic success rate and complete absorption rate between the initial nodule group and the recurrent nodule group (both P > .05). These findings

are consistent with those from a previous study conducted by Ha et al (17), where they reported that, in 11 patients who underwent lobectomy before RFA, the mean VRR at the last follow-up was 87.2%. Similarly, Kim et al (16) demonstrated that the VRR of 14 patients with benign thyroid goiter who underwent lobectomy and subsequently received TA was 85.41% ± 12.17. In our study, nodule size was not an independent factor for VRR. Subgroup analysis revealed no difference, suggesting that nodule volume did not impact the treatment outcome between the two groups. Previous studies (16,17) have found that TA is effective for small-volume nodules (<10 mL). Yan et al (18) included larger-volume nodules (15.04 mL ± 21.17) and achieved a 100% therapeutic success rate, with improvements in all nodular-related symptom and cosmetic problems. Our findings align with these results, suggesting that TA is also effective in patients with a history of thyroid surgery, regardless of nodule size. Nodule-related symptom and cosmetic scores improved significantly in both groups during the follow-up period compared with the initial conditions before TA, with no patients requiring surgery or alternative interventions after TA.

In general, patients presenting with recurrent TNs accompanied by symptoms are prioritized for thyroid surgery. Repeat operation is the standard treatment for postoperative symptomatic benign thyroid nodules. However, the presence of distortion and adhesion resulting from initial surgery poses challenges in identifying and protecting crucial neck structures during the second surgery, thereby leading to an increased incidence of complications after repeat operation, particularly recurrent laryngeal nerve injury and hypoparathyroidism. This puts surgeons in a dilemma (32,33). Referring to Medas et al (33), transient hypoparathyroidism was significantly higher after the second surgery (56.6% vs 10%) compared with the primary surgery (25.9% vs 2%), whereas transient recurrent laryngeal nerve palsy was almost four times more prevalent than in primary surgery. Calò et al (34) reported that the risk of recurrent laryngeal nerve palsy was eight times greater than that of primary surgery. A multicenter study involving 1459 patients showed all patients tolerated RFA treatment well, with a complication rate of merely 3.3% (35). Our study showed similar results, with no significant differences in complications and adverse effects between the two groups, comparable tolerance to TA treatment, and no life-threatening complications or sequelae. One patient in the initial nodule group and one in the recurrent nodule group experienced recurrent laryngeal nerve injury, which was subsequently resolved 2 and 3 months after ablation. This favorable outcome can be attributed to the following key points. First, the thermal ablation process was performed by experienced operators trained in ablation techniques. Second, real-time US was used to monitor the TA operation. Finally, the use of the hydrodissection technique and moving shot technique plays a pivotal role in mitigating potential thermal damage to critical structures, particularly in patients with a history of thyroid surgery (22,23,36).

Furthermore, it should be noted that thyroid repeat surgery may inevitably result in permanent hypothyroidism in patients, necessitating life-long supplementation with thyroid hormones, which can potentially cause irreversible damage to health (2,3,6,7). Due to real-time US monitoring during TA and protection of critical anatomic structures in the neck, hypothyroidism after TA is extremely rare (35). In this study, only one patient exhibited transient hypothyroidism after TA, with serum thyroid hormone levels returning to baseline at the 3-month follow-up visit. No patients in the initial nodule group required Unithroid (Jerome Stevens Pharmaceuticals) supplementation after ablation. No patients in the recurrent nodule group who had previously received Umetrix following initial surgery needed to escalate the drug dose after TA. Initial thyroid hormone levels exhibited no significant difference compared with those at the last follow-up after TA in both groups (both $P > .05$), indicating that TA therapy has no impact on thyroid function in patients with initial nodules or patients with recurrent nodules. This is in line with previous findings (16–18). Yan et al (18) reported that 20 patients with symptomatic BTNs who had undergone previous thyroid lobectomy maintained good thyroid function without hypothyroidism after RFA. It is concluded that TA can effectively reduce dependence on life-long medications without deteriorating thyroid function in patients with recurrent nodules. Despite the low incidence of hypothyroidism after TA, permanent hypothyroidism has been reported in some studies (17,35). Although the cause remains unclear, it has been suggested that the autoimmune thyroiditis linked to pre-existing thyroid antibodies in patients is thought to be a primary contributor (36). Therefore, it is critical to inform patients with elevated antithyroid peroxidase antibodies before ablation about the risk of hypothyroidism.

Hematomas, typically resulting from electrode-induced mechanical injury or thyroidal vasodilation–related hemorrhage, can be classified as perithyroidal, subcapsular, and intranodal. They can be controlled through a few minutes of neck pressure or hemostatic medication. Intranodal hemorrhage due to RF electrodes can often be effectively controlled by directly ablating the bleeding sites. Previous studies have also suggested that careful inspection of important anterior jugular vein or perithyroidal vessels before insertion of ablation electrodes can prevent severe perithyroidal hemorrhage. In addition, compared with large-bore electrodes, a modified small-bore electrode (18 gauge) reduces the bleeding risk (37–43).

There are several limitations to our study. First, it should be noted that this was a single-center retrospective study. Despite our diligent efforts to balance baseline features during PSM, selection bias cannot be completely eliminated. Second, the potential impact of diverse thyroid surgery methods and operator experience on patient outcomes were not considered. Third, we had a modest sample of patients with recurrent nodules who underwent thyroid surgery. Future research should focus on conducting long-term prospective multicenter studies with larger sample sizes to yield more robust evidence regarding the efficacy of TA for recurrent nodules.

In conclusion, our findings provide valuable evidence supporting the comparable safety and feasibility of TA therapy as a viable treatment option for initial and recurrent TNs. Our findings provide clinicians with a valuable reference for selecting TA as a first-line alternative treatment for patients with recurrent nodules following thyroid surgery. More significantly, our study lays the foundation for future thyroid nodule treatment guidelines to propose TA as a first-line alternative treatment option for recurrent nodules.

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