

Clinical Outcomes and Volume Reduction Predictors Following Microwave Ablation of Benign Thyroid Nodules: A Comparative Study of Solitary Nodules and Multinodular Goiters

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Rationale and Objectives: To investigate the efficacy and safety of microwave ablation (MWA) for benign thyroid nodules, including a comparison of volume reduction rates (VRR) between solitary nodules and multinodular goiters (MNG), and an assessment of autonomously functioning thyroid nodules (AFTN).

Materials and Methods: A single-center retrospective evaluation was conducted on 112 patients treated with MWA between June 2023 and June 2024. Routine ultrasound and clinical evaluations were performed at 3, 6, and 12 months postoperatively after the MWA procedure. Technical efficacy was defined as a 50% or more reduction in the initial nodule volume after ablation. Outcomes assessed included VRR, technical efficacy, complication rates, cosmetic scores, and therapeutic success for AFTN. A multiple linear regression model was employed to examine potential factors influencing the VRR.

Results: The majority of patients were female (68.48%), with a mean age of 57.84 ± 11.10 years. The median initial nodule volume was 10.66 mL. Of the 112 ablations performed, 50 (44.6%) targeted solitary nodules and 62 (55.4%) MNGs. The median VRR was 62.9% at 3 months, 80.5% at 6 months, and 88.2% at 12 months. Technical efficacy was achieved in 94.6% of nodules at 12 months. No significant difference in VRR was found between solitary nodules and MNG at any follow-up interval (12-month VRR: 89.0% vs. 87.5%, $p = 0.973$). Multivariate analysis identified the presence of calcification, nodule composition, and energy delivered per mL as significant independent predictors of the VRR ($p < 0.001$ for all). Of the 18 patients with AFTNs, 11 required antithyroid medication before treatment. Following MWA, seven of these 11 patients (63.6%) successfully discontinued medication and maintained euthyroidism, a result that was statistically significant ($p < 0.001$). There were no major complications. Transient hoarseness was observed in three patients three patients (2.7%), with no permanent deficits. Cosmetic scores showed significant improvement ($p < 0.001$).

Conclusion: MWA is an effective and safe treatment for benign thyroid nodules, demonstrating high technical efficacy and significant volume reduction for both solitary nodules and MNG. Energy delivery per mL, nodule composition, and the presence of calcification were identified as significant independent predictors of the VRR. Furthermore, MWA shows promise as a viable treatment option for AFTNs.

Key Words: Autonomously functioning thyroid nodule; Microwave ablation; Multinodular goiter; Thyroid nodules; Volume reduction rate.

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Abbreviations: **ACR-TIRADS** American College of Radiology-Thyroid Imaging Reporting and Data System, **AFTN** Autonomously Functioning Thyroid Nodule, **FNA** Fine-Needle Aspiration, **IQR** Interquartile Range, **MNG** Multinodular Goiter, **MWA** Microwave Ablation, **RFA** Radiofrequency Ablation, **T3** Triiodothyronine, **T4** Thyroxine, **TSH** Thyroid Stimulating Hormone, **VRR** Volume Reduction Rate

INTRODUCTION

Thyroid nodules are present in approximately 20–67% of the general population, with over 90% classified as benign (1,2). Nodules without high-risk features are typically managed through active surveillance. However, those exhibiting progressive growth or causing compressive symptoms may require intervention, with surgery being the primary treatment option (3). Potential risks associated with surgical approaches, such as partial or total thyroidectomy, include hypocalcemia, recurrent laryngeal nerve injury, infection, bleeding, and cosmetic concerns (4). These risks may outweigh the benefits of surgery for managing benign nodules.

Ultrasound-guided thermal ablation is a minimally invasive, non-surgical treatment that employs localized heating to induce coagulative necrosis and reduce nodule volume. The success of this approach is typically evaluated using the volume reduction rate (VRR), which is calculated by comparing nodule volume before and after treatment. Current guidelines recommend thermal ablation as an alternative to surgery for patients experiencing compressive symptoms and/or cosmetic concerns due to large benign nodules (5). This treatment can significantly reduce nodule volume and relieve associated symptoms while also offering minimal scarring and a lower risk of complications compared to surgery. While there is substantial evidence supporting the efficacy and safety of radiofrequency ablation (RFA), data on microwave ablation (MWA) remain relatively limited (6).

Moreover, the existing body of literature predominantly focuses on the treatment of solitary nodules (7–9). To our knowledge, no investigation has yet directly compared the VRR outcomes of MWA between multinodular goiters (MNG) and solitary nodules. While the evidence comparing the efficacy of RFA for VRR in these two groups is also limited, it suggests that the procedure has comparable safety and efficacy profiles for both (10,11). Furthermore, although outcomes for autonomously functioning thyroid nodules (AFTNs) treated with RFA are well-documented, research on the use of MWA for such nodules remains scarce. A direct comparative analysis of VRR between autonomously functioning and non-functioning nodules is absent from the current research landscape.

This study aimed to evaluate and compare the efficacy and safety of MWA for a broad spectrum of benign thyroid nodules, including both autonomously functioning and non-functioning nodules, across solitary and MNG presentations, over a 12-month follow-up period, with the primary outcomes being the VRR and its associated variables.

MATERIALS AND METHODS

This single-center retrospective study received approval from the Institutional Review Board (Giresun Training and Research Hospital; Approval 02.10.2024/06), which waived the requirement for informed consent. The study protocol adhered to the ethical principles outlined in the Declaration of Helsinki (1975, as revised).

Patient Selection

A cohort of 157 patients underwent ultrasound-guided MWA for thyroid nodules in our interventional radiology unit between June 2023 and June 2024. Ablation was performed per session on a single nodule for solitary nodules, or on all nodules within a single lobe for MNG. Patients were enrolled based on the following inclusion criteria: (a) no sonographic features suspicious for malignancy (anteroposterior/transverse diameter ratio > 1, microcalcifications, marked hypoechoic); (b) benign pathology confirmed by a minimum of two ultrasound-guided fine-needle aspirations (FNAs) (in MNG, FNAs targeted the dominant nodule and any nodule scoring ACR-TIRADS > 3); (c) Nodules with a maximum diameter of at least 1 cm; (d) subjective symptoms including neck discomfort, pain, compression, or cosmetic concerns; (e) documented patient refusal or clinical ineligibility for surgery; and (f) commitment to scheduled follow-up. Exclusion criteria were: (a) histologically proven malignancy; and (b) inadequate follow-up (< 12 months). Figure 1 shows the patient selection.

Pre-ablation Assessment

Ultrasonography was used to evaluate the diameters, volumes, compositions, vascularity, capsules, and presence of calcification of the nodules. Nodule volume was quantified using the formula $V = \pi abc/6$, with V representing volume in cubic centimeters or milliliters, a signifying the maximum

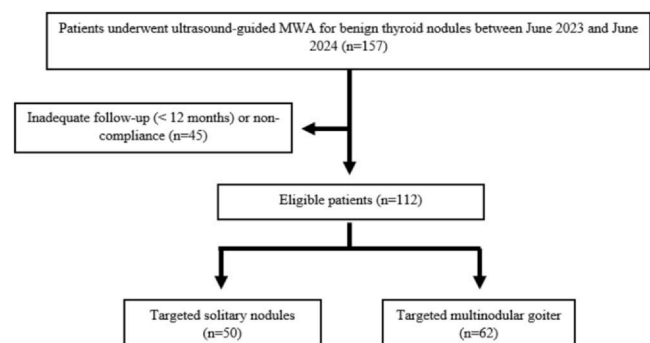


Figure 1. Patient selection.

diameter, and b and c indicating the two perpendicular diameters. For patients with MNG, the aggregate diameter of nodules was measured, and characteristics of dominant nodules were documented. The cystic fraction of the total nodule volume was calculated. Nodule composition was classified as predominantly solid (solid portion $\geq 90\%$), mixed (solid portion between 10% and 90%), or predominantly cystic. Punctate hyperechoic foci ≤ 1 mm were excluded from the calcification group, whereas macrocalcifications > 1 mm were classified as calcifications. Nodules were classified based on the presence of annular blood flow. Internal blood flow signals were graded on a scale of 0 to 3: 0 = no flow signal; 1 = 1–2 punctate flow signals; 2 = 3–4 punctate flow signals or one vessel with a clear wall; 3 = multiple vessels with a clear wall within the nodule or more than four punctate blood flow signals (12). All ultrasound images were evaluated by a radiologist with over 10 years of experience and a radiology assistant in their final year of training.

A diagnosis of an autonomously functioning thyroid nodule was made if the following criteria were met: (1) a sonographically identified thyroid nodule or MNG demonstrating hyperactivity on radioiodine scintigraphy and (2) suppressed thyroid-stimulating hormone (TSH) and normal or elevated free triiodothyronine (T3) and/or free thyroxine (T4) levels, assessed prior to any therapeutic intervention. The patients' cosmetic status was assessed using a cosmetic score: 1 = no obvious mass; 2 = palpable but not visible mass; 3 = visible mass when swallowing; 4 = obvious mass. Laboratory evaluations included measurements of T3, T4, and TSH levels, along with routine blood and coagulation tests.

MWA Procedure

All ablation procedures were performed by a radiologist with over 10 years of experience in ultrasound-guided thermal

ablation. The microwave unit consisted of a Maxblate ablation generator (Canyon Medical Inc.) and a flexible water-cooled antenna (Canyon Medical Inc. 16–18 G needle, 7–10 cm long, 3-mm active tip). The procedure was conducted with the patient lying supine and their neck in extension. Following standardized peri-procedural preparation, including cutaneous disinfection and sterile draping, 1–2% lidocaine was administered subcutaneously in the perithyroidal region. Hydrodissection was performed for all nodules, and a transisthmus approach with a moving-shot technique was adopted.

The hydrodissection procedure began with a 1 mL subcutaneous injection of 2% lidocaine for local anesthesia. Under ultrasound guidance, hydrodissection was performed using a 21-gauge needle. Initially, a 10 mL solution (5 mL of 2% lidocaine mixed with 5 mL of an iso-oncotic solution [Hydroxyethyl Starch 130/0.4, Voluven®]) was administered into the anterior compartment to establish a protective fluid barrier. Following the anterior injection, the needle position was carefully adjusted—using a transthyroidal approach when necessary—to access the posterior compartment without full withdrawal. An additional 10 mL of iso-oncotic solution was then injected posteriorly to isolate critical structures, including the recurrent laryngeal nerve and esophagus (Fig 2). Real-time ultrasound confirmed optimal fluid distribution in both compartments, with the iso-oncotic solution providing sustained protection during ablation due to its colloid properties. Post-procedure, patients were monitored for possible allergic reactions.

An output power range of 30–40 W was routinely utilized during ablation procedures. Ablation continued until hyperechoic sonographic changes filled the entire nodule or nodules. The ablation time, total energy delivered, and energy delivered per mL (energy delivered per mL = Energy (J)/initial volume (mL)) were recorded. For predominantly cystic or mixed nodules, the procedural sequence was

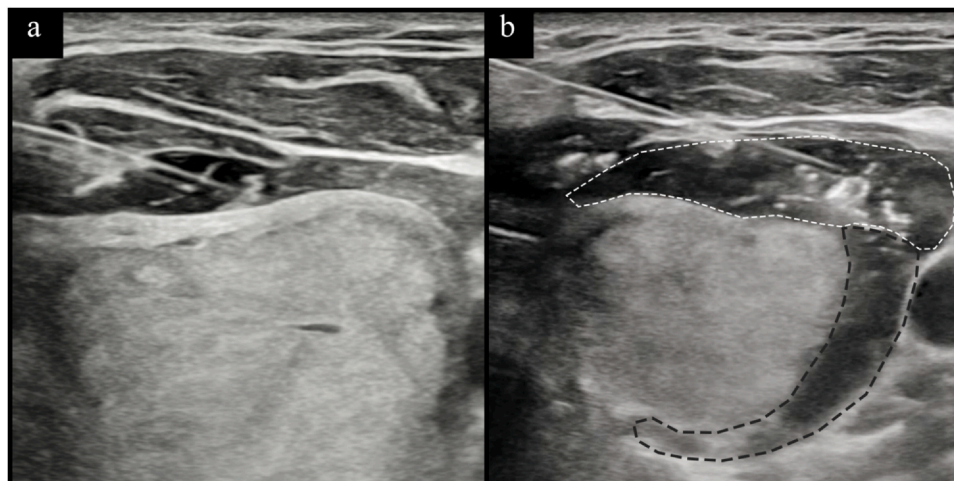


Figure 2. Ultrasound-guided hydrodissection technique. (a) Zoomed view demonstrating the placement of a fine-needle anterior to the thyroid capsule and the injection of 10 mL of solution (5 mL of 2% lidocaine mixed with 5 mL of an iso-oncotic solution) into the anterior compartment. (b) Following needle repositioning, an additional 10 mL of iso-oncotic solution is injected to expand both the anterior (white dotted area) and posterior (black dotted area) compartments, achieving isolation of the critical structures.

modified to mitigate bleeding risk: initial ablation was performed prior to fluid aspiration. This approach leverages the coagulative effects of thermal energy to seal vessels within the nodule wall, thus minimizing the risk of hemorrhage upon decompression. Subsequently, the evacuated cystic cavity was re-ablated to ensure complete treatment of any residual solid component and the peripheral margin. Complications and side effects occurring during or after the procedure were classified according to the criteria established by the International Working Group on Image-Guided Tumor Ablation (13). Major complications—defined as those occurring during or post-procedure that threatened life if untreated, posed significant morbidity/disability risks, or required prolonged hospitalization—were designated as such. All other complications were classified as minor. Untreated adverse outcomes not necessitating medications or therapeutic intervention were defined as side effects. Following MWA, patients were monitored in the hospital for 2 h for signs of discomfort or complications and were discharged after post-procedural follow-up.

Outcome Measures

Patients demonstrating full compliance with the 3-month, 6-month, and 12-month assessments were included in the efficacy analysis. Nodule diameters and volumes were evaluated using identical methodology pre- and post-ablation. The primary efficacy endpoint was the VRR, calculated as: $VRR = [(Initial\ Volume - Current\ Volume) / Initial\ Volume] \times 100\%$. Technical efficacy was defined as a $\geq 50\%$ reduction in initial nodule volume post-ablation. Energy per ablated volume was calculated as the total energy delivered divided by the volume reduction achieved during the procedure: $Energy\ (J) / (Initial\ Volume - Post-Procedural\ Volume)\ (mL)$. Functional therapeutic success refers to the achievement of euthyroidism without the necessity of medication. Complications were recorded in terms of number and percentage. Patient cosmetic scores were reassessed at the 3-month, 6-month, and 12-month follow-up visits. Pre-procedure, 3–6, and 12-month follow-up grayscale ultrasound images of a representative cases are shown in Figures 3–5.

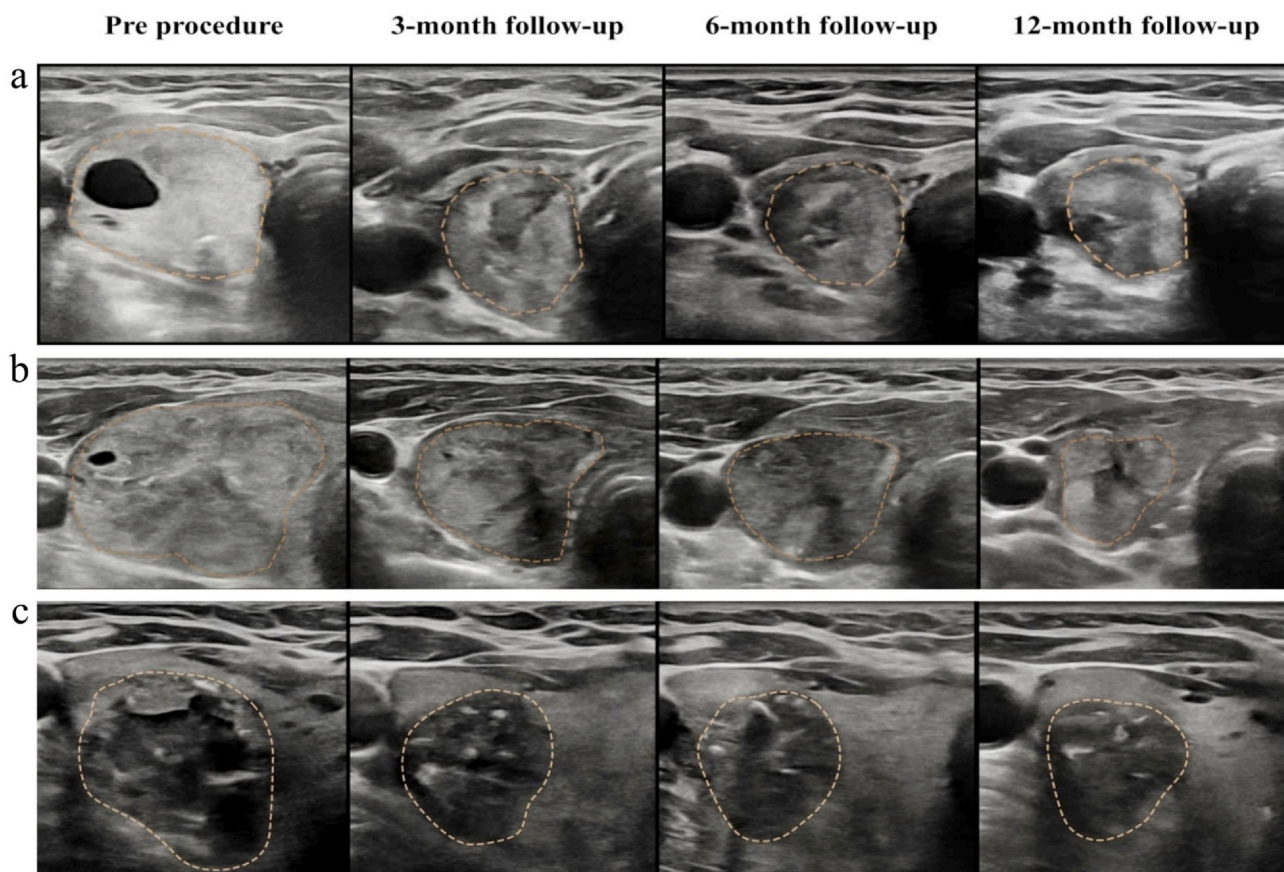


Figure 3. Representative grayscale ultrasound images obtained preprocedurally and at 3, 6, and 12 months postprocedurally. **(a)** A mixed solitary nodule in the right thyroid lobe of a 63-year-old female. Preprocedural volume was 6.1 mL (26 × 25 × 18 mm), which was reduced to 0.5 mL (10 × 11 × 9 mm) at 12 months, corresponding to a 91% volume reduction. The cosmetic score improved from 3 at baseline to 1 at the 12-month follow-up. **(b)** A multinodular goiter in the right lobe of a 66-year-old female. Preprocedural volume was 8.1 mL (34 × 24 × 19 mm), which was reduced to 1.2 mL (16 × 12 × 12 mm) at the 12-month follow-up, an 85% reduction. The cosmetic score improved from 4 to 1. **(c)** A solitary nodule with macrocalcifications in the right lobe of a 68-year-old female. Preprocedural volume was 8.4 mL (35 × 23 × 20 mm), which was reduced to 2.3 mL (20 × 16 × 14 mm) by the 12-month evaluation, a 73% reduction. The cosmetic score improved from 3 to 1.

Statistical Analysis

Statistical analyses were conducted using SPSS version 22.0 (IBM Corp., Armonk, NY). Normality of the data was assessed by Kolmogorov–Smirnov test. Normally distributed continuous variables are expressed as mean \pm standard deviation, while non-normally distributed data are reported as median and interquartile range (IQR). VRR and associated factors were assessed at postoperative follow-up intervals of 3, 6, and 12 months. Nonparametric comparisons employed the Mann–Whitney U test for two-group analyses and the Kruskal–Wallis test for multi-group comparisons. Relationships between continuous variables were assessed using Pearson's correlation coefficient. Variables demonstrating univariate associations with VRR at the 6-month follow-up ($p < 0.1$) were entered into a multiple linear regression model to identify potential predictors. Statistical significance was defined as $p < 0.05$.

RESULTS

Out of the 157 patients, 112 met our study criteria. The remaining 45 patients were excluded for the following reasons: 12 had only attended their 3-month follow-up, and 11 had only attended their 6-month follow-up. Although 22 patients had completed their 12-month follow-up examination, they had not attended their 3-month and/or 6-month visits. All patients requested treatment for symptoms such as compression, cosmetic concerns, or ATFNs. Among those included in the study, 75 (66.9%) were female. The mean patient age was 57.84 ± 11.10 years (range 33–86 years). Of the 112 ablations performed, 50 (44.6%) targeted solitary nodules and 62 (55.4%) MNG. The mean ablation time was 13.75 ± 4.53 min. The baseline characteristics of the patients, detailed sonographic features of the nodules, and procedural energy data for the entire cohort are summarized in [Table 1](#). The table also presents comparative analyses between patients with solitary nodules and MNGs.

Technical efficacy was achieved in 82 (73.2%) of the 112 patients at three months, in 100 (89.3%) at six months, and in 106 (94.6%) at 12 months. Of the six patients that did not reach technical efficacy, three were from the solitary and three were from the MNG group. The median nodule volume was 10.66 mL (IQR: 4.45–24.02) before the procedure, which decreased to 3.32 mL (IQR: 1.03–7.82) at three months, 1.88 mL (IQR: 0.54–4.82) at six months, and 1.24 mL (IQR: 0.30–3.29) at 12 months. The median VRR was 62.9% at three months, 80.5% at six months, and 88.2% at 12 months. There was no statistically significant difference in the VRR between solitary nodules and MNGs at 3, 6, and 12 months (68.1% vs. 62.4% at month 3, $p = 0.804$; 79.0% vs. 82.4% at month 6, $p = 0.998$; 89.0% vs. 87.5% at month 12, $p = 0.973$).

Eighteen patients (seven with solitary nodules and 11 with MNG) with ATFNs underwent MWA. Of these, 11 patients (four with solitary nodules and seven with MNG; 61.1%)

required pretreatment with antithyroid medication. At the 12-month follow-up, seven patients (three with solitary nodules and four with MNG) had achieved euthyroidism and discontinued medication, a statistically significant therapeutic outcome ($p < 0.001$). VRR did not differ significantly between ATFNs and non-functioning nodules at 3 months (65.1% vs. 62.8%; $p = 0.801$), 6 months (84.0% vs. 79.2%; $p = 0.126$), or 12 months (88.9% vs. 87.4%; $p = 0.488$).

Relationship Between Technical Parameters and VRR

A significantly higher median energy per mL was delivered in procedures where technical efficacy was achieved (1252.0 J/mL, $n = 106$) compared to those where it was not achieved (596.5 J/mL, $n = 6$; $p = 0.007$). Furthermore, a positive correlation was observed between the energy delivered per mL and VRRs ($r = 0.382$, $p < 0.001$). An evaluation of nodule characteristics indicated that composition and calcification were significant factors influencing energy efficiency. Mainly solid nodules required a higher energy per ablated volume compared to cystic or mixed nodules (1465.9 J/mL vs. 1242.4 J/mL, $p = 0.026$). Nodules containing calcification demanded a significantly greater energy per ablated volume than non-calcified nodules (1996.6 J/mL vs. 1353.1 J/mL, $p < 0.001$). Other features, including gender, location, capsular presence, vascularity score, and annular vascularity, did not demonstrate a statistically significant impact on energy requirements ([Table 2](#)).

Predictors of Volume Reduction

We performed a univariate analysis that incorporated various factors, including gender, nodule location, MNG presence (versus solitary), nodule composition, presence of a capsule, vascularity score, annular vascularity, calcification, pre-procedure nodule volume, total delivered energy, energy delivered per mL, and procedure time. Nodule composition, the presence of calcification, and energy delivered per mL were found to significantly affect the 12-month VRR ($p = 0.014$, $p = 0.003$, and $p < 0.001$, respectively). A subsequent multivariate analysis confirmed that nodule composition, the presence of calcification, and energy delivered per mL had a statistically significant impact on the VRR ($p < 0.001$ for all). [Figure 4](#) displays line graphs illustrating the relationship between categorical variables and the median nodule VRR. [Table 3](#) presents the detailed results of the univariate and multivariate analyses.

Cosmetic Outcomes

The mean cosmetic score for patients was 2.58 ± 1.15 prior to the procedure, 1.64 ± 0.86 at the three-month post-procedure check-up, 1.52 ± 0.84 at six months, and 1.48 ± 0.85 at 12 months. There was a statistically significant difference in cosmetic scores before and after the procedure ($p < 0.001$).

TABLE 1. The Baseline Characteristics of the Patients and Nodules, and Procedural Energy Data

Patient Characteristics	All	Solitary	MNG	p-value
Age	57.84 ± 11.10	58.52 ± 10.66	56.27 ± 11.77	0.293
Gender				0.415
Female	75 (67%)	36 (72%)	39 (62.9%)	
Male	37 (33%)	14 (28%)	23 (37.1%)	
Thyroid Function				
TSH	1.12 ± 0.93	1.32 ± 1.06	1.02 ± 0.64	0.070
T3	3.10 ± 0.65	2.99 ± 0.67	3.25 ± 0.66	0.112
T4	1.16 ± 0.20	1.14 ± 0.21	1.17 ± 0.20	0.397
Nodule Features				
Location				0.725
Left lobe	46 (41.1%)	22 (44%)	24 (38.7%)	
Right lobe	52 (46.5%)	23 (46%)	29 (46.8%)	
Isthmus	14 (12.5%)	5 (10%)	9 (14.5%)	
Composition				0.262
Mainly solid	76 (67.9%)	35 (70%)	50 (80.6%)	
Mainly cystic or mixed	36 (32.1%)	15 (30%)	12 (19.4%)	
Capsule Presence				0.193
Present	26 (23.2%)	15 (30%)	11 (17.7%)	
Absent	86 (76.8%)	35 (70%)	51 (82.3%)	
Vascularity score				0.117
0	28 (25%)	16 (32.0%)	12 (19.4%)	
1	34 (30.4%)	11 (22.0%)	23 (37.1%)	
2	32 (28.5%)	13 (26.0%)	19 (30.6%)	
3	18 (16.1%)	10 (20.0%)	8 (12.9%)	
Annular flow				0.445
Present	39 (34.8%)	20 (40.0%)	19 (30.6%)	
Absent	73 (65.9%)	30 (60.0%)	43 (69.4%)	
Calcification				
Present	22 (19.6%)	8 (16%)	14 (22.6%)	0.225
Absent	90 (80.4%)	42 (84%)	48 (77.4%)	
Functioning				
Non-functioning	94 (83.9%)	43 (86%)	51 (82.3%)	0.753
Autonomously functioning	18 (16.1%)	7 (14%)	11 (17.7%)	
Maximum diameter (mm)	35.00 (25.50–45.50)	28.5 (20.2–40.0)	37.0 (32.0–49.8)	0.001
Preoperative volume (mL)	10.66 (4.45–24.02)	5.53 (2.27–20.39)	11.58 (7.39–27.41)	0.002
Energy data				
Total energy delivered	11023 (4421–29591)	6017 (3420–21808)	14796 (8562–38972)	0.001
Energy delivered per mL	1220 (943–1482)	1252 (955–1424)	1164 (867–1519)	0.613

MNG, multinodular goiter. Age and thyroid function test results are presented as mean ± standard deviation, while maximum diameter, preoperative volume, and energy data are presented as median with interquartile range.

Complication Rates

There were no major complications. Transient hoarseness occurred in only three patients (one with a solitary nodule and two with MNG), representing 2.7% of the entire cohort. This condition resolved within one week. Minor hemorrhages occurred subcutaneously or intramuscularly in 13 patients; all were minor complications that resolved spontaneously within one week. Eight patients reported post-procedural pain as a side effect, and two patients experienced a vasovagal reaction during the procedure, both of which resolved without treatment. The overall minor complication and side effect rates were 14.3% and 8.9%, respectively.

DISCUSSION

Our study demonstrated that MWA is an effective and safe treatment for benign thyroid nodules, including AFTNs and MNG. Among the 112 patients who underwent MWA, no major complications were observed. Transient hoarseness was noted in three patients (2.7% of the cohort). The median VRR of the treated nodules was 62.9% at 3 months, 80.5% at 6 months, and 88.2% at 12 months post-ablation. Technical efficacy was achieved in 73.2% of nodules at three months, 89.3% at six months, and 94.6% at 12 months. No significant difference in VRR or technical efficacy was observed between solitary nodules and those within an MNG.

TABLE 2. Association of Nodule Characteristics with Energy Delivery Parameters

Variable	Energy per mL	p	Energy per Ablated mL	p
Gender		0.618		0.906
Male	1322.0 (955.0–1425.0)		1430.9 (1106.2–1676.5)	
Female	1156.0 (908.0–1512.5)		1412.2 (1078.1–1847.6)	
Solitary or MNG		0.613		0.580
Solitary	1252.0 (955.2–1424.8)		1421.5 (1062.7–1921.1)	
MNG	1164.5 (867.0–1519.5)		1432.4 (1134.6–1726.0)	
Location		0.448		0.657
Right lobe	1170.5 (936.0–1414.2)		1409.3 (1102.7–1625.7)	
Left lobe	1313.5 (949.8–1616.2)		1469.0 (1081.0–1856.0)	
Isthmus	1138.5 (885.2–1473.0)		1482.8 (1100.2–1806.2)	
Composition		0.375		0.026
Mainly solid	1252.0 (952.0–1472.0)		1465.9 (1201.7–1846.0)	
Cystic or mixed	981.0 (825.0–1468.5)		1242.4 (980.2–1612.8)	
Capsule Presence		0.586		0.368
Present	1290.0 (952.8–1521.5)		1442.9 (1243.6–1809.8)	
Absent	1181.0 (896.5–1424.8)		1423.3 (1055.6–1781.0)	
Vascularity score		0.701		0.806
0	1041.5 (934.5–1515.2)		1369.7 (1028.2–1769.0)	
1	1223.5 (955.0–1410.2)		1403.8 (1165.6–1663.1)	
2	1257.0 (931.5–1448.5)		1440.0 (1184.4–1659.4)	
3	1384.0 (868.5–1681.8)		1548.2 (1183.9–1932.2)	
Annular Flow		0.282		0.482
Present	1258.0 (955.0–1547.5)		1415.7 (1252.2–1768.3)	
Absent	1177.0 (882.0–1424.0)		1430.9 (1052.8–1788.2)	
Calcification		0.056		< 0.001
Present	1347.5 (1000.0–1822.0)		1996.6 (1461.4–2341.7)	
Absent	1155.5 (898.0–1424.8)		1353.1 (1037.8–1626.6)	
Functioning		0.158		0.355
Non-functioning	1177.0 (928.0–1425.0)		1407.0 (1092.4–1759.3)	
Autonomously functioning	1363.5 (992.5–1745.5)		1469.0 (1312.9–1845.5)	

MNG, multinodular goiter. Energy data are presented as median with interquartile range.

MWA was performed on 18 patients with AFTNs. Of the 11 patients (61%) using antithyroid drugs prior to the procedure, only four (22%) required them 12 months post-ablation. Furthermore, patients reported significant improvement in cosmetic scores.

Studies from various countries investigating the use of MWA for treating benign thyroid nodules have reported a VRR of approximately 40–80% at three months, 48–86% at six months, and 75–90% at 12 months (7–9,12,14–17). These variations may be attributed to differences in nodule size and characteristics or the array of instruments and techniques used. Our results are broadly consistent with this documented range. It is noteworthy that the technical efficacy rates in these studies, including the multicenter study by Cang et al. (12) (87.3% at six months and 90.5% at 12 months) and the study by Yue et al. (9) (82.3% at 6 months), were defined using the same criterion as in our study—a VRR of $\geq 50\%$. Consequently, the technical efficacy results from our study are directly comparable to and align with those reported in the literature.

Our study also included patients with MNG. As far as we are aware, this is the first study to compare the VRR between MNG and solitary thyroid nodules treated with

MWA, demonstrating comparable outcomes. The VRR and complication rates in patients with MNG were similar to those observed in patients with solitary nodules. There are currently no specific MWA studies related to MNG in the literature. Guo et al. (10) reported a 90.9% VRR at 12 months, and a 2.7% complication rate in their RFA study of patients with MNG. Lang et al. (11) reported similar safety and efficacy in patients with MNG compared to those with solitary nodules in their RFA study. Our MWA results demonstrate high efficacy in both solitary nodules (VRR 79.0%) and MNG (VRR 82.4%) at 6 months, consistent with Lang et al.'s (11) RFA findings (solitary: 77.29%, MNG: 73.38%); this comparable efficacy was maintained at the 12-month follow-up, with VRRs of 89.0% for solitary nodules and 87.5% for MNG. These findings suggest that MWA is a robust technique equally effective for both solitary nodules and the more complex anatomy of MNG, challenging the perception that multinodularity may be a limiting factor for ablation. The high VRR achieved in MNG indicates that MWA can induce substantial necrosis across multiple nodules, offering a viable minimally invasive treatment option.

Our findings on the critical role of energy delivery per unit volume are strongly supported by, yet also refine, the

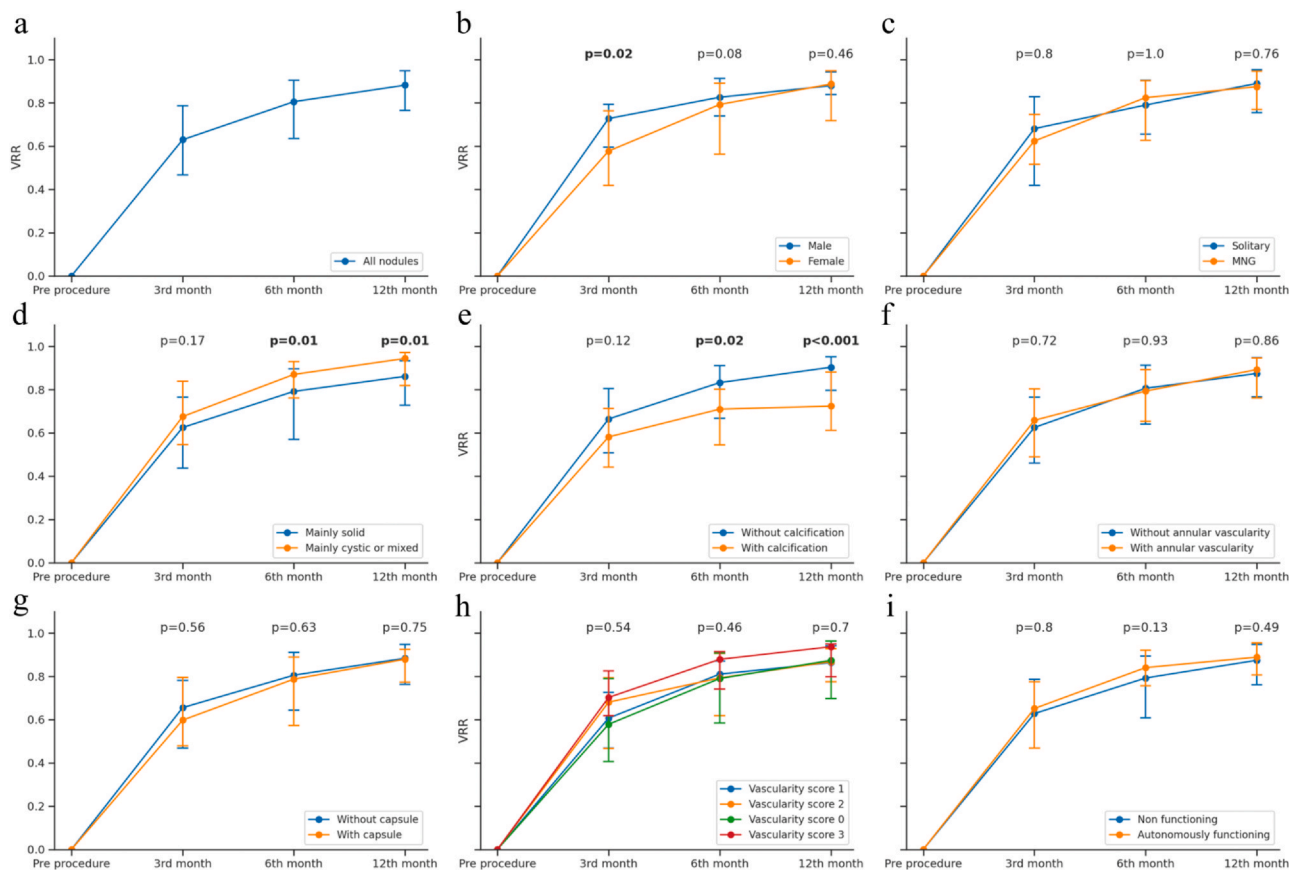


Figure 4. VRR of treated nodules. (a) Line graph depicting the VRR over time for all nodules. (b–i) Line graphs illustrating the relationship between VRR and the following variables: (b) gender, (c) multinodular goiter vs. solitary, (d) composition, (e) presence of calcification, (f) presence of annular vascularity, (g) presence of capsule, (h) vascularity score, and (i) functioning status.

existing literature. The positive correlation we observed between energy per mL and VRR directly aligns with the results of Korkusuz et al. (18), who reported a very strong correlation between total energy and absolute volume reduction. More significantly, our data corroborate the key conclusion of Mei et al. (19) that energy per mL is a primary determinant of efficacy, while total energy and ablation time are not. Furthermore, our identified median energy of 1252.0 J/mL for technically effective procedures falls precisely within the 784–2274 J/mL range that Mei et al. established as necessary for achieving a VRR $\geq 75\%$, providing external validation for their model. Our study extends these previous findings by demonstrating that this energy requirement is not uniform but is significantly modulated by specific nodule composition. The fact that solid and calcified nodules required substantially higher energy per mL (1465.9 J/mL and 1996.6 J/mL, respectively) offers a mechanistic explanation for the observation by Mei et al. that calcification was an independent negative predictor of efficacy. The higher energy demand in solid nodules also aligns with the trend reported by Korkusuz et al., who found the highest mean $E/\Delta V$ in solid nodules compared to complex and cystic nodules. Therefore, our results consolidate the literature by quantitatively confirming that achieving a

sufficient energy density is paramount for efficacy and that preprocedural planning must account for nodule composition, particularly the presence of solid tissue or calcification, to optimize energy delivery and ensure successful ablation outcomes.

Several studies have investigated factors related to the VRR in thermal ablation treatments. Some have associated the initial characteristics of thyroid nodules with the efficacy of RFA (20–22). Likewise, some studies on MWA have argued that initial volume and solidity are associated with the VRR (7,9,12,23–25). In our study, solid nodules exhibited significantly lower VRRs compared to mixed-cystic nodules at all follow-up intervals, with a statistically significant difference observed at both 6 and 12 months ($p = 0.01$). Multivariate analysis further confirmed nodule composition as an independent predictor of VRR. These findings are consistent with prior MWA studies by Luo et al. (24) and Khanh et al. (25), who also reported inferior volume reduction in solid nodules. In contrast to our results, which showed no significant correlation between pre-ablation volume and VRR, Cang et al. (12) reported higher VRRs in nodules exceeding 20 mL. Although the studies by Luo et al. (24) and Khanh et al. (25) support our finding of no significant association between initial volume and VRR, these

TABLE 3. Univariate Analysis of Factors Associated with VRR at 12 Months

Categorical variables	Median %VRR (IQR)	Univariate Analysis		Multivariate Analysis	
		Test	p	Coefficient	p
Gender		Mann-Whitney U	0.205		
Male	87.9 (83.9–94.3)				
Female	88.7 (71.7–94.8)				
Location		Kruskal-Wallis	0.450		
Right lobe	87.5 (77.7–93.8)				
Left lobe	89.3 (76.8–94.9)				
Isthmus	89.8 (65.2–94.6)				
Solitary or MNG		Mann-Whitney U	0.973		
Solitary	89 (75.4–95.4)				
MNG	87.5 (76.9–94.6)				
Composition		Mann-Whitney U	0.014	0.066	< 0.001
Mainly solid	86.1 (72.8–93.3)				
Mainly cystic or mixed	94.4 (81.8–97.1)				
Capsule presence		Mann-Whitney U	0.605		
Present	87.9 (77.4–92.5)				
Absent	88.4 (76.3–94.9)				
Vascularity score		Kruskal-Wallis	0.814		
0	87.4 (69.8–96.3)				
1	86.4 (77.5–94.2)				
2	86.8 (77.5–92.7)				
3	93.7 (79.8–94.9)				
Annular flow		Mann-Whitney U	0.931		
Present	79.3 (65.4–89.3)				
Absent	80.6 (64–91.2)				
Calcification		Mann-Whitney U	0.003	0.146	< 0.001
Present	72.4 (61.2–88)				
Absent	90.3 (79.7–95.2)				
Functioning		Mann-Whitney U	0.488		
Non-functioning	87.4 (76.1–94.7)				
Autonomously functioning	88.9 (80.6–95.5)				
Continuous variables	Correlation coefficient	Test	p		
Age	0.052 (–0.133 to 0.236)	Pearson	0.579		
Total Energy delivered	0.141 (–0.045 to 0.318)	Pearson	0.138		
Energy delivered per mL	0.382 (0.211–0.530)	Pearson	< 0.001	0.0002	< 0.001
Time	0.141 (–0.045 to 0.318)	Pearson	0.136		
Preoperative Volume	–0.051 (–0.234 to 0.135)	Pearson	0.590		

MNG, multinodular goiter; VRR, volume reduction rate; IQR, interquartile range

divergent findings highlight the complex interplay of factors influencing ablation efficacy. Therefore, the impact of pre-ablation nodule volume on MWA outcomes remains controversial and warrants further investigation.

We further evaluated the impact of sonographic features—including capsule presence, intranodular vascularity, and peripheral ring-type vascularity—on VRR. Capsule status showed no relation to VRR, consistent with Cang et al. (12). Although nodules with high intranodular vascularity (score 3) exhibited a trend toward greater VRR, neither vascularity score stratification nor peripheral ring-type vascularity significantly related to VRR. This contrasts with

Luo et al. (24), who observed reduced VRR exclusively in nodules with peripheral vascularity at 3 months—a finding not sustained at later intervals or in their 12-month multivariate analysis. Collectively, our vascularity results reflect broader literature trends showing limited predictive value of these features for ablation outcomes.

Our study investigated the effect of the presence of calcification on the VRR of thyroid nodules. In nodules with calcification, the VRR was significantly lower at the six- and 12-month follow-ups compared to nodules without calcification, a difference that was statistically significant. Furthermore, multivariate analysis revealed that the presence

of calcification was an independent predictor of lower VRR. To date, only a limited number of studies have examined the impact of calcification on VRR following the thermal ablation of thyroid nodules. In a study of 52 nodules with calcifications treated with RFA, Li et al. (26) found that hard macrocalcifications exhibiting acoustic shadowing were associated with a lower VRR than soft calcifications. Mei et al. (19) defined a VRR exceeding 75% as indicative of treatment efficacy in their MWA study. Their analysis demonstrated that nodules with calcifications exhibited reduced efficacy, identifying calcification as an independent predictor of lower treatment efficacy. Calcification may reduce treatment efficacy by adversely affecting energy distribution and heat production during thermal ablation. Additionally, acoustic shadowing caused by calcifications can complicate needle positioning and the execution of the moving-shot technique. These factors may explain the reduced VRR observed in calcified nodules within our cohort.

Eighteen patients with autonomously functioning nodules were included in our study. Before the procedure, 11 patients (61%) were using antithyroid medication, but this requirement ceased for 7 of 11 patients (63%) at 12 months post-procedure. In Erturk et al.'s (27) study, which compared the efficacy of radioactive iodine treatment and MWA in nodules exhibiting autonomous function, therapeutic success was achieved in 18 (60%) of the 30 nodules treated with MWA. Our findings are consistent with this. To our knowledge, we compared for the first time the VRR of autonomously functioning nodules with that of non-functioning nodules and found them to be similar. However, both our study and previous studies had small sample sizes, making the success of MWA in autonomously functioning nodules controversial.

During the follow-up period, the patients demonstrated significant improvements in cosmetic scores, which were consistent with the observed VRR. A statistically significant difference was found between the cosmetic scores at the start of treatment and at follow-up. The improvements in cosmetic scores observed after treatment were comparable to those reported in other studies (12,14). Our overall complication profile and incidence rates are consistent with those reported in the literature; however, a notable distinction was the absence of major complications (12,14,28,29). Our technique deviated from conventional practice in two key aspects, which may explain our favorable safety profile. First, we employed an iso-oncotic solution for hydrodissection. Its colloidal properties provide sustained protective separation of critical structures, a feature we attribute to the absence of permanent hoarseness in our cohort. Second, for predominantly cystic nodules, aspiration of the internal contents was deliberately performed following the ablation procedure rather than preceding it. We hypothesize that this modification prevented intranodular bleeding by allowing the coagulative effects of the thermal energy to seal vessels prior to decompression.

This study has several limitations. First, its non-randomized, retrospective design inherently introduces the potential for selection bias. Consequently, future randomized prospective studies are required to validate these findings. Second, the sample size, though adequate for the primary analysis, was limited in key subgroups—such as patients with AFTNs—potentially constraining the statistical power for these specific comparative analyses. Third, the follow-up period was of intermediate duration. However, extant literature confirms that the VRR peaks at three months, undergoes significant continued reduction through six months, and substantially plateaus by 12 months (28,29). Therefore, our 12-month findings offer valuable preliminary insights. Finally, the single-center nature of this study may affect the generalizability and reproducibility of the results.

In conclusion, MWA represents a viable therapeutic approach for benign thyroid nodules, demonstrating favorable safety and efficacy profiles in clinical practice. In our study, a VRR of up to 88% and technical efficacy rates of up to 95% were achieved 12 months after ablation, with significant improvements observed in the cosmetic scores of the patients. MWA is also a promising option for managing ATFNs and MNG, particularly in patients unsuitable for surgery. Further prospective, multicenter studies with extended follow-up are warranted to validate and expand upon these findings.

ETHICAL APPROVAL

This retrospective study received approval from the Institutional Review Board (Giresun Education and Research Hospital; Approval BAEK-129, 02.10.2024/06), which waived the requirement for informed consent. The study protocol adhered to the ethical principles outlined in the Declaration of Helsinki (1975, as revised).

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CREDIT AUTHORSHIP CONTRIBUTION STATEMENT

Uluhan Eryuruk: Writing – original draft, Visualization, Methodology, Investigation, Data curation, Conceptualization. **Tumay Bekci:** Writing – review & editing, Supervision, Methodology, Investigation, Data curation. **Mehmet Tonkaz:** Visualization, Methodology, Investigation, Formal analysis. **Merve Nur Tasdemir:** Writing – original draft, Visualization, Data curation. **Yasemin Emur Gunay:** Investigation, Data curation. **Oguz Dikbas:** Investigation, Formal analysis, Data curation.

INFORMED CONSENT

Due to its retrospective design, we waived the requirement for informed consent.

DECLARATION OF COMPETING INTERESTS

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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