

The Efficacy of Ultrasound-Guided Microwave Ablation for Benign Thyroid Nodules and the Correlation Analysis of Its Influencing Factors

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Abstract

Objective: To evaluate the efficacy of ultrasound-guided microwave ablation (MWA) for benign thyroid nodules and analyze related influencing factors. **Methods:** Ninety-five patients with 96 benign thyroid nodules underwent MWA under ultrasound guidance. Follow-up examinations at 1, 3, and 6 months included two-dimensional ultrasound, color Doppler, and contrast-enhanced ultrasound to assess nodule volume reduction and ablation success. Influencing factors such as age, gender, nodule size, type, and ablation parameters were analyzed using Spearman's correlation and multiple regression analysis. **Results:** MWA showed significant efficacy with most nodules reducing in volume or disappearing ($P < 0.05$). The average volume reduction ratios (VRR) at 1, 3, and 6 months were $52.98\% \pm 22.23\%$, $68.18\% \pm 19.81\%$, and $82.39\% \pm 15.03\%$, respectively, with 95.8% of nodules achieving VRR > 50%. Cystic nodules had the most significant volume reduction. Initial nodule volume, blood flow status, nodule composition, and energy absorption per unit volume significantly influenced VRR ($P < 0.05$), while age, gender, and ablation duration did not ($P > 0.05$). **Conclusion:** MWA is an effective minimally invasive treatment for benign thyroid nodules, with efficacy influenced by initial nodule volume, composition, blood flow, and ablation energy.

Keywords Ultrasonography; MWA; Thyroid benign nodules; VRR; Influencing factors

The diagnostic rate for thyroid nodules, a commonly encountered endocrine disorder in clinical practice, has significantly increased with the widespread utilization of ultrasound imaging techniques^{1–3}. It has been estimated that the incidence of thyroid nodules in the adult population can reach as high as 50%–60%⁴, with the majority being benign.

Although most benign thyroid nodules do not require active treatment, surgical intervention remains a viable option in cases where the nodule is large enough to cause compression symptoms, aesthetic concerns, or psychological burden on the patient⁵. However, traditional surgical treatments, such as partial or total thyroidectomy, may entail risks such as hoarseness, hand-foot cramping, and cervical scars, and require general anesthesia with a relatively prolonged postoperative recovery period⁶.

With the advancement of medical technology, minimally invasive procedures have increasingly become a focus of research. Among these, ultrasound-guided microwave ablation (MWA) has shown great potential for the treatment of benign thyroid nodules due to its minimal invasion, rapid recovery, and significant therapeutic effects^{7–9}. Microwave ablation involves the generation of high temperatures locally to utilize microwave energy, resulting in coagulative necrosis of the tissue and the elimination of the nodule. Moreover, MWA can be performed under local anesthesia, thereby reducing the risks associated with general anesthesia and being particularly suitable for patients who cannot tolerate general anesthesia^{7,10,11}.

Numerous domestic and international guidelines and expert consensus statements have recommended MWA as an effective treatment for benign thyroid nodules. For instance, the 2015 American Thyroid Association (ATA) guidelines indicate that MWA may be considered for patients with contraindications to surgery or those who refuse surgical treatment^{12,13}. In 2016, the European Thyroid Association (ETA) also recommended MWA as an alternative to surgery¹².

However, the efficacy of microwave ablation is influenced by various factors, including the nature, size, location, and blood flow of the nodule^{14,15}. To further enhance the therapeutic efficacy of microwave ablation and reduce complications, in-depth analysis of these influencing factors is crucial. Therefore, the purpose of this study is to evaluate the efficacy of ultrasound-guided microwave ablation in the treatment of benign thyroid nodules and to analyze the factors that influence treatment outcomes, with the aim of providing robust references and guidance for clinical practice.

1 General Data

The data for this study comprised 95 patients with a total of 96 nodules, selected from the University of Hong Kong–Shenzhen Hospital from April 2022 to December 2023. The inclusion criteria were as follows: The patient must meet one or two of the following criteria:

- (1) Ultrasound suggests benign.
- (2) Patients whose medical conditions preclude surgical treatment or who decline surgical treatment.
- (3) Simultaneously meet one of the following conditions:

- (a) Autonomous functional nodules causing hyperthyroidism symptoms.
- (b) Patient's psychological burden is too heavy to affect their normal life and they refuse clinical observation (the patient requires minimally invasive interventional treatment).
- (c) Patients experiencing a self-reported symptom associated with the nodule (e.g., foreign body sensation, discomfort or pain in the neck, etc.) or a nodule that affects appearance, and requires treatment.
- (4) All patients signed the informed consent form for this study.

Exclusion criteria:

- (1) Patients with a giant retrosternal thyroid gland or those with thyroid nodules predominantly located posterior to the sternum (as relative contraindications, subdivided ablation may be considered).
- (2) The thyroid nodule contains coarse calcification.
- (3) The sound-producing muscle function on the opposite side of the lesion is abnormal.
- (4) Patients with severe disorders of the coagulation mechanism.
- (4) Patients with severe cardiopulmonary disease.

The data consisted of patients aged 18–73 years, with a mean age of 44.54 ± 12.59 years. There were 22 male patients and 67 female patients. Among them, 27 nodules had a maximum diameter of less than 3 cm, and 28 nodules had a maximum diameter of more than 3 cm. There were 39 solid nodules, 28 nodules with mixed solid and cystic components, and 26 cystic nodules.

2 Methods

2.1 US Technique

The study utilized a Mindray Resona 7OB color Doppler ultrasound platform with a non-linear transducer that had an acquisition frequency of 3–9 MHz to image the subjects. The subjects should lie flat without a pillow to expose the anterior neck adequately. Following this, a two-dimensional ultrasound examination is conducted, performing comprehensive longitudinal and transverse sectional scans of the thyroid. The size, location, ultrasound grayscale characteristics, and color Doppler ultrasound features of the nodules are recorded in detail using medical terminology.

2.2 Ablation Device

Nanjing Kangyou Co., Ltd. offers the KY-2000 microwave ablation system along with the KY-2450A disposable microwave ablation needle. The microwave ablation (MWA) procedure for the target nodules is described as follows:

- (1) Preoperative routine examinations, including thyroid function tests, coagulation profile, laryngoscopy, and electrocardiogram, were conducted. Fine-needle aspiration (FNA) was performed specifically for the nodules to confirm a benign pathology.

(2) Patients were positioned in the supine position with cervical extension, and electrocardiographic monitoring devices were connected. Venous access was established for the administration of contrast agent, if necessary.

(3) Thyroid two-dimensional ultrasound (gray-scale and color Doppler flow imaging (CDFI)), contrast-enhanced ultrasound (CEUS), were performed to examine the nodules, record their ultrasound characteristics, and measure the longest (L), widest (W), and deepest (D) diameters.

(4) The neck skin was disinfected and prepared, and 2% lidocaine hydrochloride was used for local layer-by-layer anesthesia. If the nodule contained cystic fluid, the fluid was aspirated using a syringe before MWA (Figure 1).

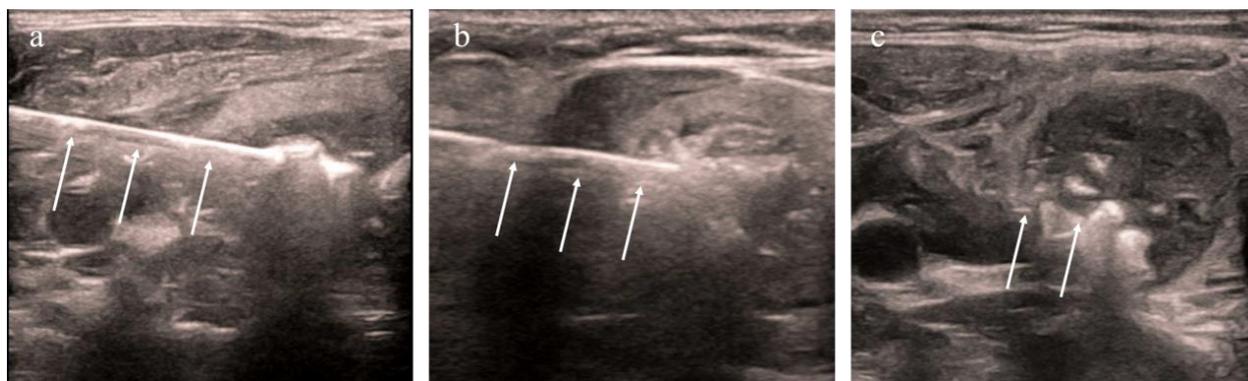


Figure 1. Intraoperative ultrasound-guided imaging of a thyroid nodule with different components. The arrow indicates the areas for ablation in a) a cystic-dominant nodule, b) a cystic-solid nodule, and c) a solid-dominant nodule, under real-time ultrasound guidance.

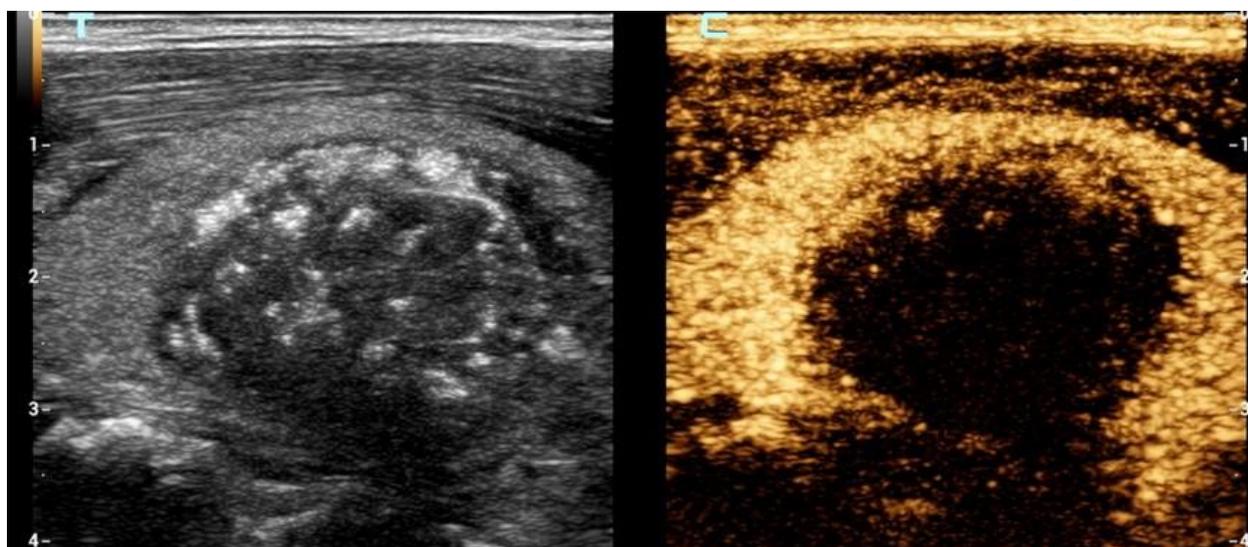


Figure 2. Postoperative contrast-enhanced imaging demonstrates that the original thyroid nodule exhibits no contrast agent enhancement.

(5) Physiological saline was injected into the spaces between the thyroid, carotid artery, trachea, esophagus, and posterior thyroid space (laryngeal nerve area) to create a “liquid isolation band.”

(6) The output power of the MWA instrument was set within the range of 25W–35W. The skin was punctured, and the MWA needle was accurately directed into the nodule under ultrasound guidance using the “moving ablation” technique. The nodule was completely covered by a strong echoic gasification area, and no blood flow signals were observed within the nodule on color Doppler imaging; ablation was then stopped.

(7) CEUS was performed immediately after MWA to confirm the ablation area. If there was any residual enhanced area, supplemental ablation was conducted until the nodule was completely without enhancement (Figure 2).

(8) Ice compresses were applied to the puncture site for 6 hours post-procedure to minimize edema and discomfort.

2.3 Experiments

Pre-operative and at 1, 3, and 6 months post-operation, two-dimensional ultrasound, color Doppler, and contrast-enhanced ultrasound examinations were conducted on benign thyroid nodules undergoing ablation at different time points. Recordings were made of the nodule composition, pre-operative nodule volume, color blood flow grading, and the volume of the nodule at the time of follow-up examinations at 1, 3, and 6 months post-operation. The volume reduction ratio (VRR) was calculated, and the ablation power used and duration were recorded to calculate the unit volume ablation energy. The correlation between VRR and nodule composition, blood flow grading, and pre-operative nodule size was analyzed.

2.4 Evaluation Metrics

In this study, the VRR was used as the primary metric to evaluate the efficacy of ablation. The criteria for assessment are as follows:

- (1) Complete nodule disappearance and cure: $VRR = 100\%$
- (2) Significant surgical effect: $VRR \geq 50\%$
- (3) Improvement after surgical treatment: $25\% \leq VRR < 50\%$
- (4) Ineffective treatment: $VRR < 25\%$
- (5) Recurrence: Increase in nodule volume or appearance of new nodules.

The VRR is calculated using the following formula:

(1) Volume of the Ablated Nodule (cm^3)

$$V = \frac{\pi}{6} \times a \times b \times c$$

Note: The units for the three diameters (a, b, c) are in centimeters (cm).

(2) Volume Reduction Ratio (VRR)

$$VRR = \left(\frac{\text{Baseline volume} - \text{Post-operative follow-up volume}}{\text{Baseline volume}} \right) \times 100\%$$

(3) Ablation Energy Density

Additionally, the parameter “Ablation Energy Density” was employed to analyze the relationship between energy delivery and VRR. The specific calculation formula is as follows:

$$\frac{\text{Set Ablation Power} \times \text{Ablation Duration}}{\text{Initial volume of the nodule}}$$

To evaluate the blood supply of the target nodule, Adler’s blood flow grading system was utilized (Figure 3):

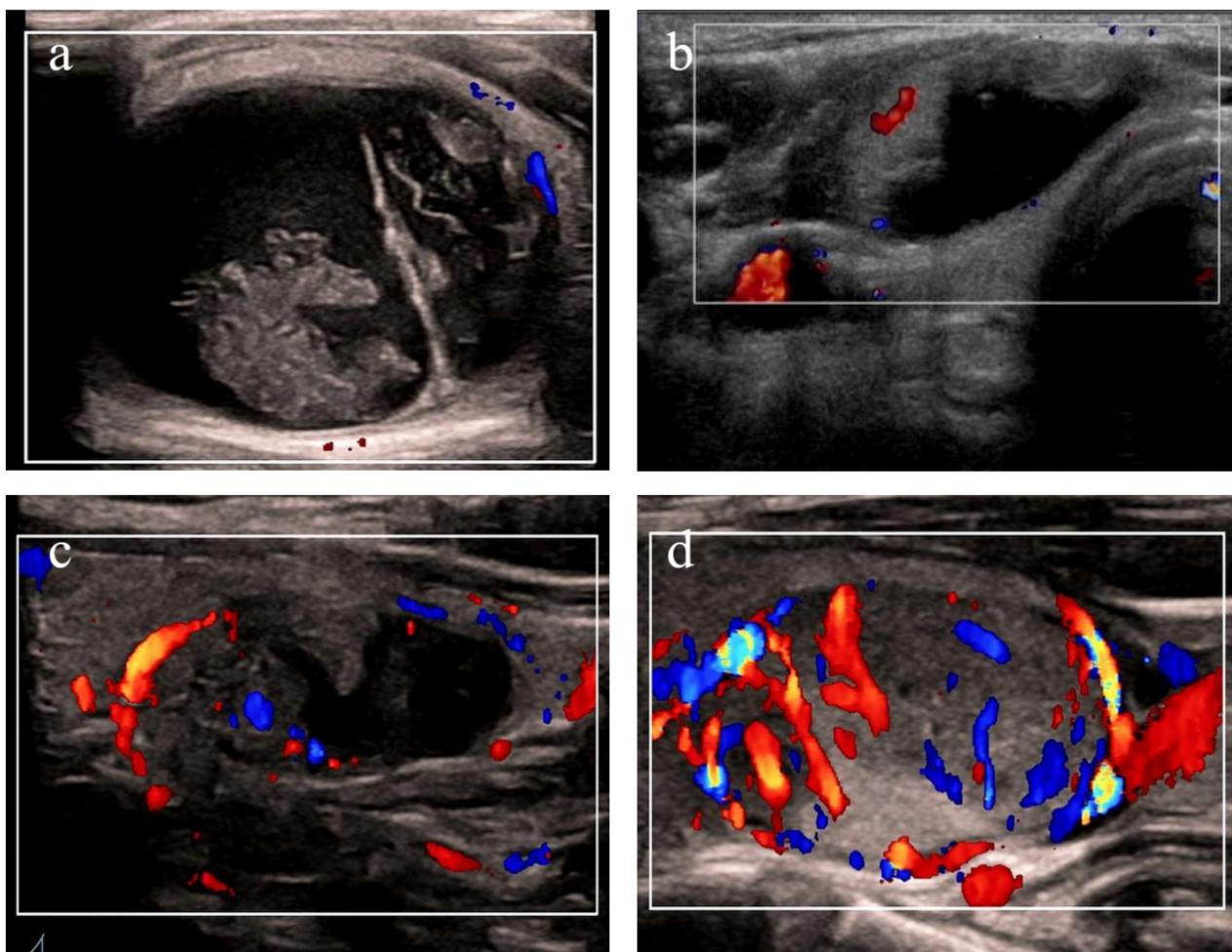


Figure 3. The grading of blood flow in thyroid nodules. a) Grade 0 thyroid nodule blood flow, no obvious blood flow signal within the nodule; b) Grade I thyroid nodule blood flow, 1 to 2 punctate blood flow signals visible within the nodule; c) Grade II thyroid nodule blood flow, multiple punctate blood flow signals visible within the nodule; d) Grade III thyroid nodule blood flow, abundant blood flow signals within the nodule.

- (1) Grade 0: Rare or no blood flow signal.
- (2) Grade I: Mild blood flow signal, with 1 to 2 punctate or small vessels visible.
- (3) Grade II: Moderate blood flow signal, with 3 to 4 punctate vessels or one longer vessel

entering the nodule.

(4) Grade III: Rich blood flow signal, with 5 or more punctate vessels or two longer vessels visible.

Nodules were further categorized based on their cystic and solid components as follows:

- 1) Solid group: Cystic component < 20%
- 2) Cystic-solid group: Cystic component > 20%, < 80%
- 3) Cystic group: Cystic component > 80%.

3 Statistical Methods

Excel software was used to organize the data, and SPSS 26.0 statistical software was employed for data analysis. Measurement data are expressed as mean \pm standard deviation (SD). After the Shapiro-Wilk (S-W) test, some measurement data showed a non-normal distribution. Data with a skewed distribution are represented by medians and interquartile ranges (IQR). Comparisons between two groups were performed using the Kruskal-Wallis test, while intragroup comparisons at various time points were conducted using the Friedman test. Pairwise comparisons of time points were performed using the Wilcoxon test. Correlation analysis was performed using the Spearman correlation coefficient. A significance level of $P < 0.05$ was considered statistically significant.

4 Results

Table 1 shows the characteristics of the study group patients, including 95 patients with a total of 96 nodules. There were 22 males and 67 females, aged between 23 and 77 years, with an average age of 44.54 ± 12.59 years. The nodules comprised solid nodules (40), solid-cystic nodules (28), and cystic nodules (28). Among them, there were 66 small nodules (≤ 10 ml), 24 medium-sized nodules (11-30 mL), and 6 large nodules (> 30 ml), with an average volume of 6.89 (2.82, 11.73) ml. The average ablation time was 248.50 (172.25, 428.00) seconds. Six patients experienced intraoperative pain, and there were no cases of postoperative bleeding, infection, or nerve functional damage (Table 2).

The volume changes and reduction rates of nodules with different compositions at 1 month, 3 months, and 6 months postoperatively are shown in Tables 3 and 4. Out of the 96 nodules, 96.9% (93/96) showed a significant treatment effect at 6 months postoperatively (VRR > 50%). The largest volume of nodules with a solid composition before operation was approximately 55.14 mL, the largest volume of cystic-solid nodules was about 67.78 mL, and the largest volume of cystic nodules was 56.96 mL. The volume of all three groups gradually decreased at each time point after operation, with the cystic group showing the most significant reduction, followed by the cystic-solid group, and the solid group showing the slowest volume reduction, all with statistical significance ($P < 0.05$) (Table 3). The VRR of the solid group, cystic-solid group, and cystic group increased at 1, 3, and 6 months postoperatively, with the cystic group having the

Table 1. Baseline Characteristics of Patients

Number of patients/nodules	95/96
Sex (male/female)	22/67
Age (years)	44.54 (12.59)
Ablation Duration(s) (P50 (P25, P75))	248.50 (172.25, 428.00)
Nodule volume at baseline (mL) (P50 (P25, P75))	6.89 (2.82, 11.73)
Small nodules (≤ 10 mL) (%)	66 (68.75)
Medium nodules (11–30 mL) (%)	24 (25.00)
Large nodules (> 30 mL) (%)	6 (6.25)

Table 2. Complications Occurrence

	Pain	Infection	Bleeding	Recurrent Laryngeal Nerve Injury	Skin Injury	Hypocalcemia
Number of cases	6	0	0	0	0	0
Incidence Rate (%)	6.74%	0%	0%	0%	0%	0%

highest VRR, the solid group the lowest, and the cystic-solid group in between, all showing statistical significance ($P < 0.05$) (Table 4).

Table 3. Distribution of Volume Change at Various Time Points Among Three Groups (P50 (P25, P75))

Group	<i>n</i>	Preoperative	POM 1M	POM 3M	POM 6M	χ^2	<i>P</i>
Solid group	40	4.64(2.07,11.00)	3.11(1.32,6.96) ^a	1.93(0.81,4.95) ^{ab}	1.03(0.28,3.64) ^{abc}	113.78	<0.01
Cystic-solid group	28	7.83(4.66,11.18)	2.68(1.51,4.96) ^a	1.36(0.91,3.47) ^{ab}	1.00(0.50,2.87) ^{abc}	76.98	<0.01
Cystic group	28	8.88(3.23,15.02)	2.01(1.26,3.87) ^a	0.85(0.41,2.45) ^{ab}	0.30(0.19,1.17) ^{abc}	81.11	<0.01
<i>Z</i>	-	4.63	2.07	5.37	10.59		
<i>P</i>	-	0.10	0.36	0.07	0.005		

Notes: “a” denotes a significant difference from the preoperative value at $P < 0.05$. “b” indicates a significant difference from the postoperative 1-month value at $P < 0.05$. “c” signifies a significant difference from the postoperative 3-month value at $P < 0.05$.

The analysis of the correlation between the VRR and various influencing factors at different

Table 4. Distribution of Shrinkage Rates at Various Time Points Among Three Groups (P50 (P25, P75))

Group	n	POM 1M	POM 3M	POM 6M	χ^2	P
Solid group	40	0.40(0.23,0.52) ^a	0.57(0.44,0.66) ^a	0.76(0.63,0.91) ^{ab}	69.95	<0.01
Cystic-solid group	28	0.65(0.52,0.76) ^a	0.80(0.70,0.88) ^a	0.88(0.80,0.93) ^{ab}	45.51	<0.01
Cystic group	28	0.68(0.57,0.81) ^a	0.82(0.66,0.93) ^a	0.95(0.86,0.98) ^{ab}	49.00	<0.01
Z	-	34.48	24.67	24.16	-	-
P	-	0.000	0.000	0.000	-	-

Notes: a indicates that the comparison at the specified time point with the preoperative value was significant at $P < 0.05$. b indicates that the comparison at the specified time point with the postoperative 1-month value was significant at $P < 0.05$.

time points for all 96 nodules revealed that nodule blood flow status ($P < 0.05$), initial size of the nodule ($P < 0.05$), cystic-solid grade of the nodule ($P < 0.05$), and the energy delivery per unit volume ($P < 0.05$) were significantly associated with VRR at 1 month and 3 months postoperatively. At 1 month postoperatively, the blood flow grade was negatively correlated with VRR, while nodule size was positively correlated with VRR. At 3 months postoperatively, the blood flow grade remained negatively correlated with VRR, and nodule size remained positively correlated with VRR. At 6 months postoperatively, the ablation duration was negatively correlated with VRR, and the blood flow grade was also negatively correlated with VRR. No other factors showed a significant correlation with VRR (Table 5).

Table 5. Analysis of the Correlation between Different Influencing Factors and the Nodule Shrinkage Rate

Grouping	Spearman Correlation	Age	Ablation Power	Ablation Duration	Blood Flow Grade	Nodule Size	Nodule Cystic-Solidity Score	Ablation Energy Density
POM 1M	r	0.028	-0.033	-0.060	-0.458	0.359	0.596	-0.267
	P	0.789	0.752	0.558	0.000	0.000	0.000	0.009
POM 3M	r	0.064	0.106	-0.112	-0.402	0.264	0.521	-0.437
	P	0.535	0.302	0.779	0.000	0.009	0.000	0.000
POM 6M	r	0.130	0.045	-0.277	-0.417	0.053	0.411	-0.289
	P	0.208	0.661	0.006	0.000	0.606	0.000	0.004

5 Discussion

The results of this study indicate that MWA is an effective and safe minimally invasive treatment option for benign thyroid nodules. Analysis of 96 benign thyroid nodules from 95 patients revealed that MWA significantly reduced nodule volume, with complete disappearance observed in most cases. This outcome is consistent with previous studies^{10, 11}, further confirming the clinical value of MWA in the treatment of thyroid nodules.

The study demonstrated that post-ablation nodule volume reduction increased over time. The volume reduction rate was 0.40 (0.23, 0.52) for solid nodules, 0.65 (0.52, 0.76) for cystic-solid nodules, and 0.68 (0.57, 0.81) for cystic nodules at one month post-operatively. At three months, the reduction rates were 0.57 (0.44, 0.66) for solid nodules, 0.80 (0.70, 0.88) for cystic-solid nodules, and 0.82 (0.66, 0.93) for cystic nodules. At six months, the reduction rates were 0.76 (0.63, 0.91) for solid nodules, 0.88 (0.80, 0.93) for cystic-solid nodules, and 0.95 (0.86, 0.98) for cystic nodules, aligning with the reports of Feng B¹⁰ and Heck et al¹⁶.

Furthermore, cystic-solid and cystic nodules exhibited greater reduction rates than solid nodules at all post-operative time points, corroborating the findings of Mo et al¹⁷. This may be due to the pre-ablation aspiration of cyst fluid in non-solid nodules, resulting in a more rapid decrease in nodule volume post-operatively.

The study also identified initial nodule volume, blood flow status, nodule composition, and energy absorption per unit volume as crucial factors influencing the efficacy of MWA. Notably, energy absorption per unit volume had the most significant impact on nodule volume reduction. At one and three months post-operatively, blood flow grade was inversely correlated with volume reduction rate (VRR), while nodule size was positively correlated with VRR. This suggests that higher peripheral blood flow may enhance the efficiency of matter absorption and metabolism post-ablation.

A direct comparison of energy grade and VRR at various post-ablation time points revealed no significant correlation ($P > 0.05$). This may be attributed to the need for a comprehensive consideration of various factors such as nodule size, nature, and location relative to the danger triangle during the selection of ablation energy parameters in actual procedures. For smaller nodules, those with a cystic nature, or those located close to the danger triangle, an initial energy setting of 25W-30W was generally chosen. This implies that the selection of initial energy in MWA is not solely based on nodule size, and the changes in post-operative VRR do not directly reflect the absorption rate of energy in different nodules, overlooking the effects of ablation duration, nodule volume, and cystic-solid nature.

To address this, the study used the parameter "Ablation Energy Density" to analyze the relationship between energy and VRR. The analysis found a significant correlation between post-operative VRR and the energy of ablation per unit volume ($P < 0.05$). It is worth noting that factors such as patient age, gender, and ablation duration had no significant correlation with treatment efficacy ($P > 0.05$). This suggests that the efficacy of MWA in treating benign thyroid nodules is not influenced by patient demographic differences but primarily depends on the biolog-

ical characteristics of the nodules and technical parameters during the ablation process. However, it is necessary to conduct further studies on specific populations (such as elderly patients, pediatric patients, pregnant women, etc.) to determine the safety and efficacy of MWA in these groups.

Although microwave ablation (MWA) shows significant efficacy in the treatment of benign thyroid nodules, this study has certain limitations. Firstly, as a retrospective study, it may be subject to selection bias. Future research should involve prospective randomized controlled trials to further validate our findings. Secondly, the relatively small sample size and limited follow-up period may affect the generalizability and long-term evaluation of results. Therefore, future studies should aim to increase the sample size and extend the follow-up period to more accurately assess the long-term efficacy of MWA in treating benign thyroid nodules.

6 Conclusion

This study analyzed the clinical data and ultrasound examination data of 95 patients with benign thyroid nodules, confirming the correlation between various influencing factors and the ablation efficacy. The initial volume of the nodule, blood flow status, nodule composition, and energy absorption per unit volume are important factors affecting the efficacy of MWA. This finding emphasizes the critical importance of precisely controlling the ablation energy during the MWA treatment process to optimize therapeutic outcomes. Furthermore, preoperative evaluation of the blood flow status of the nodule can assist clinical physicians and patients in predicting postoperative outcomes.

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