Am J Transl Res 2021;13(12):13723-13731
www.ajtr.org /ISSN:1943-8141/AJTR0135382

Original Article

Ultrasound-guided microwave ablation of benign thyroid nodules: effects on inflammatory factors and thyroid function

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Received May 18, 2021; Accepted August 23, 2021; Epub December 15, 2021; Published December 30, 2021

Abstract: Objective: To explore the effects of ultrasound-guided microwave ablation on inflammatory factors and thyroid function in patients with benign thyroid nodules. Methods: A total of 150 patients with benign thyroid nodules treated in the Huazhong University of Science and Technology Union Shenzhen Hospital from January 2017 to December 2018 were selected as research participants, with 75 patients in each group. Patients in the control group received traditional surgery, while those in the study group were treated with ultrasound-guided percutaneous microwave ablation. The two groups were compared in terms of the following: clinical effect, quality of life scores, white blood cell count (WBC), hypersensitive-C-reactive-protein (hsCRP), tumor necrosis factor α (TNF-α), interleukin (IL)-6, epinephrine (E), norepinephrine (NE), visual analogue scale (VAS) scores, and serum levels of thyroid stimulating hormone (TSH), FT3, FT4, and TT4. Results: The total effective rate of the study group was significantly higher than that of the control group (96.00% vs. 77.33%). Before operation, there was no significant difference in WBC, VAS score, or the levels of hs-CRP, TNF-α, IL-6, E, and NE between the two groups (all P>0.05); After operation, WBC, and the levels of hs-CRP, TNF-α, IL-6, E, and NE increased significantly in both groups and were lower in the study group (all P<0.05). The nodule volume in the study group decreased with time. The serum levels of TSH, FT3, FT4, and TT4 in the study group were better than those in the control group (P<0.05). The study group obtained a lower incidence of postoperative complications than the control group (4.00% vs. 14.00%). In addition, the cosmetic score was higher and the symptom score was lower in the study group compared with the control group (all P<0.05). Conclusion: In patients with benign thyroid nodules, the ultrasound-guided microwave ablation could effectively reduce nodule volume, preserve thyroid function, and improve the quality of patients' daily life. This is closely related to a reduced inflammatory response.

Keywords: Ultrasound guidance, microwave ablation, benign thyroid nodule, clinical effect

Introduction

A thyroid nodule refers to a lump formed after abnormal proliferation of thyroid cells, that moves with the swallowing action of the patient [1-3]. Clinically, it falls into the category of multiple diseases, and the benign thyroid nodules may be single or multiple nodules [4]. The main etiologic factors of this disease are excessive or low iodine intake, long-term consumption of substances that cause goiter, long-term use of related drugs or thyroid hormone synthase, nodular goiter, or inflammatory nodule [5-7]. In non-iodine-deficient areas, 5% of female patients and 1% of male patients are diagnosed by palpation, while the detection rate on high-frequency ultrasound can be as high as 19%-67% [8-10]. Due to the rather hidden clinical manifestations of benign thyroid nodules in the early stage, patients are usually diagnosed after obvious discomfort or the presence of pathologic appearance, which often requires surgical treatment [11]. Surgical resection is considered the main traditional treatment for thyroid nodules. However, traditional surgery has been criticized for deficiencies such as large trauma, possible damage to the peripheral vessels and nerve, surgical scars of 6-8 cm on the neck, frequent postoperative hypothyroidism in many cases, and the

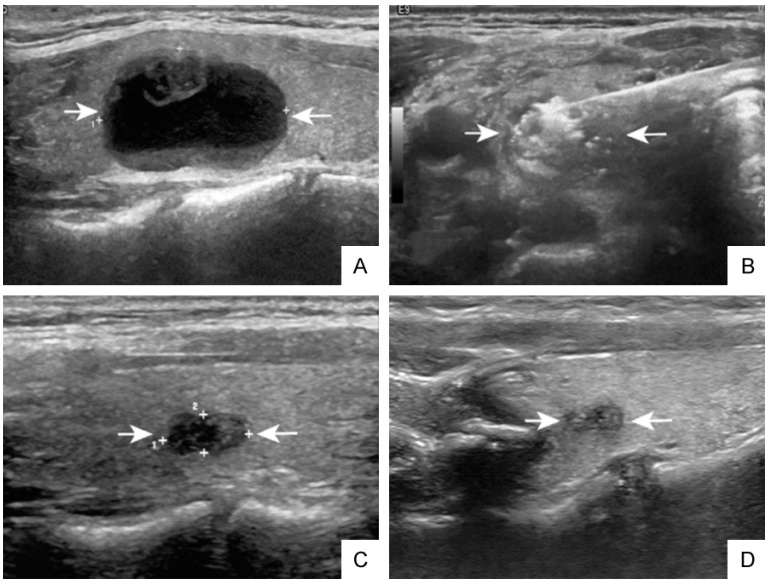

Figure 1. The typical imaging before and after the microwave ablation. A. Before RFA, conventional ultrasound showed that the nodules were mixed with cystic solid and large nodules; B. During ablation, the ablation area is hyperechoic; C. The volume of the nodules decreased three months after ablation; D. Six months after ablation, the original ablation area remained, and the volume of the nodules decreased by more than 90%.

need for regular oral administration of thyroid hormones [12, 13]. Therefore, alternative therapy that is safe, less traumatic, effective, and with smaller or no scars has always been one of the research goals of thyroid surgery. Given the small thyroid volume, the complicated relationship to adjacent organs, and the low tumor clearance rate, the clinical efficacy of ultrasound-guided microwave therapy is still controversial [14]. Accordingly, this study compared the clinical effects of the two methods.

Materials and methods

Clinical materials

A total of 150 patients with benign thyroid nodules admitted to the Huazhong University of Science and Technology Union Shenzhen Hospital from January 2017 to December 2018 were selected as the research participants and assigned to a study group (n=75) and a control group (n=75). Allenrolled patients signed an informed consent form after being fully informed of the process and purpose of the study. This protocol was approved by the Ethics Committee of the Huazhong University of Science and Technology Union Shenzhen Hospital (2016HZ12-547).

Methods

In the control group, the deep cervical fascia was longitudinally incised to isolate the anterior cervical muscle group for complete exposure of the thyroid gland. Subtotal thyroidectomy was performed by the refined capsule anatomy, followed by routine insertion and suture of the thyroid. Patients in the study group received ultrasound-guided percutaneous microwave ablation: The patient lay in a supine position with shoulders raised horizontally to fully expose the neck. First, the thyroid and lymph nodes of the patient were inspected to determine the lesion size, number, and shape, and then color Doppler ultrasound was performed to determine the blood flow inside and around the thyroid nodules. After routine disinfection and local anesthesia with 1% lidocaine, the patient's lesion was punctured under the guidance of ultrasound, with a preset output power of 40 W and a conventional ablation time of 40 s. Position and direction of the needle insertion: The needle was inserted into the middle and lower 1/3 part of the mass without intervening in the tracheal. During the puncture, the needle tip remained within the scope of ultrasonic observation. If solid nodules were detected, microwave ablation was directly applied. If the nodules were cystic, the cyst contents were removed with a syringe, and then microwave ablation of the lesion was performed. At the end of the procedure, an adhesion bandage was applied to the incision and the patient was instructed to press with their hand for 15 min. Illustration of the procedure of microwave ablation is shown in **Figure 1**.

Observation indexes

The clinical effects, scores of visual analogue scale (VAS) and quality of life (dimensions: social function, mental state, physical function, and role function), operation time, intraoperative blood loss, hospital stay, and postoperative complications were compared between

Table 1. General information of patients in the two groups

Categories	Study group	Control group	P
Gender			0.243
Male	28	29	
Female	22	21	
Average age	42.3±4.6	42.4±4.3	0.220
Disease type			0.754
Multiple nodules	29	27	
Single nodules	21	23	

the two groups. White blood cell count (WBC) as well as serum levels of hypersensitive-C-reactive-protein (hsCRP), tumor necrosis factor α (TNF-α), interleukin (IL)-6, epinephrine (E), norepinephrine (NE), thyroid stimulating hormone (TSH), FT3, FT4, and TT4 were also compared. Evaluation criteria for clinical effects: Cured: The patient's lesions were removed as indicated by ultrasound, the clinical symptoms disappeared completely, and the thyroid function indicators returned to normal; Significantly effective: The patient's lesion was removed as indicated by ultrasound, the clinical symptoms were significantly resolved, and the thyroid function indicators were basically back to normal; Effective: The patient's lesions were basically removed as indicated by ultrasound, the clinical symptoms alleviated, and the thyroid function indicators improved; Ineffective: The patients' lesions remained as indicated by ultrasound, and the clinical symptoms did not resolve or even worsened. The symptom score and cosmetic score were used to evaluate the severity of symptoms and beauty satisfaction in the two groups of patients after surgery [15]. The higher the symptom score, the more severe the symptoms of the patients; the higher the cosmetic score, the higher the beauty satisfaction.

Statistical treatment

SPSS was used for data analysis in this study. Count data were expressed as n (%), and the comparison between the two groups was performed by χ^2. The measurement data, all conforming to the normal distribution, were expressed as ($\bar{x}$ ±s), and analyzed by t-test and paired t-test. P<0.05 indicates a significant difference.

Results

Comparison of general data

In the study group, there were 28 males and 22 females with a mean age of (42.3±4.6) years old; 29 cases had multiple nodules, and 21 cases had single nodules, with an average diameter of (2.1±0.4) cm. In the control group, the male to female ratio was 29:21, and the average age was (42.4±4.3) years old; there were 29 cases of multiple nodules, and 23 cases of single nodules, with an average diameter of (2.0±0.5) cm. The two groups showed no significant difference in general information (P>0.05) **Table 1**.

Comparison of clinical efficacy

In the study group, there were 34 cases of cured, 18 cases of significantly effective, 20 cases of effective, and 3 cases of ineffective, with a total effective rate of 96.00%. In the control group, there were 19 cases of cured, 13 cases of significantly effective, 26 cases of effective, and 17 cases of ineffective, with a total effective rate of 77.33%. The total effective rate of the study group was significantly higher than that of the control group (P<0.05) **Table 2**.

Comparison of life index scores

In the study group, the mental state score was (95.02±7.13), the social function score was (93.06±4.16), the physical function score was (94.28±4.86), and the role function score was (96.01±4.03). In the control group, the scores of mental state, social function, physical function and role function were (83.17±4.64), (84.12±5.25), (84.73±6.02), and (84.72±3.10), respectively. The life index scores in the study group were all higher than those in the control group, and the differences were statistically significant (P<0.05) **Table 3**.

Comparison of perioperative indicators

In the study group, the operation time was (29.42±5.15) min, the intraoperative blood loss was (12.36±2.09) mL, and the hospitalization time was (1.52±0.29) d. In the control group, the operation time was (79.24± 12.52) min, the intraoperative blood loss was (29.42±4.84) mL, and the hospitalization time

Table 2. Efficacy of two groups (n)

Group	n	Cured	Significantly effective	Effective	Ineffective	Total effective rate [n (%)]
Study group	75	34	18	20	3	72 (96.00)
Control group	75	19	13	26	17	58 (77.33)
χ^2						6.924
P						0.012

Table 3. Life index scores of patients in the two groups

Group	n	Mental state	Social function	Physical function	Role function
Study group	75	95.02±7.13	93.06±4.16	94.28±4.86	96.01±4.03
Control group	75	83.17±4.64	84.12±5.25	84.73±6.02	84.72±3.10
t		5.263	5.973	6.014	4.052
P		0.003	0.012	0.016	0.005

Table 4. Perioperative indicators of patients in the two groups

Group	n	Operation (min)	blood loss (mL)	Hospitalization time (d)
Study group	75	29.42±5.15	12.36±2.09	1.52±0.29
Control group	75	79.24±12.52	29.42±4.84	4.01±1.23
t		4.217	6.363	5.241
P		0.021	0.001	0.004

was (4.01±1.23) d. The perioperative indicators of the study group were all better than those of the control group (P<0.05) **Table 4**.

Comparison of stress response indicators and VAS scores

Before operation, there was no significant difference in WBC and the serum levels of hs-CRP, TNF-α, IL-6, N, and NE between the two groups (P>0.05); After operation, the above indicators increased significantly (P<0.05), with lower results observed in the study group (P<0.05), as shown in **Table 5**. After operation, the VAS score of the study group was (2.37±0.36) points, which was lower than that of the control group (6.53±1.18 points), with a significant difference between the two groups (P<0.05) **Figure 2**.

Comparison of nodular reduction in the study group

In the study group, the mean volume of nodules decreased significantly with time, with the size of (2.83±1.05) cm^3 preoperatively, (2.51±0.42) cm^3 at 1 week after surgery, (2.18±0.32) cm^3 at 1 month after surgery, (1.79±0.38) cm^3 at 3 months after surgery, (1.52±0.24) cm^3 at 6 months after surgery, and (0.85±0.17) cm^3 at 12 months after surgery. The volume reduction rates at 1 week, 1 month, 3 months, 6 months, and 12 months after surgery were (13.13±7.12)%, (26.18±9.56)%, (44.59±14.74)%, (54.61±15.23)%, and (65.32±12.97)%, respectively. In the control group, the mean volume of nodules decreased from (2.72±0.88) cm^3 to (0.22±0.06) cm^3 at 1 week after surgery, and then remained stable with no new nodules. Up to 6 months after surgery, the nodules in the study group were still larger than those in the control group, with significant differences between the two groups (all P<0.001) **Figures 3** and **4**.

Comparison of thyroid function indicators

The serum levels of TSH, FT3, FT4, and TT4 in the study group were (5.02±0.84) mU/L, (2.46±0.32) nmol/L, (88.39±11.36) nmol/L, and (91.39±14.63) nmol/L, respectively, while those in the control group were (8.39±1.35) mU/L, (1.84±0.44) nmol/L, (66.39±9.25) nmol/L, and (73.25±11.25) nmol/L, respectively. The thyroid function indicators of the study group were all better than the control group (P<0.05) **Table 6**.

Comparison of functional recovery time and hospitalization time

The recovery time of thyroid biochemical indexes of the study group and control group was

Table 5. Stress response indicators of patients in the two groups

	WBC (×10°/L)		hs-CRP (mg/L)		TNF-α (ng/L)		IL-6 (ng/L)		E (ng/L)		NE (ng/mL)	
	1 d before operation	8 h after operation	1 d before operation	8 h after operation	1 d before operation	8 h after operation	1 d before operation	8 h after operation	1 d before operation	8 h after operation	1 d before operation	8 h after operation
Study group	5.67±1.03	6.15±1.03	0.68±0.40	1.85±1.11	35.14±4.72	41.52±10.13	3.01±1.12	3.35±2.08	47.56±9.54	58.25±9.26	263.25±35.22	277.25±40.25
Control group	5.53±1.26	6.72±1.16	0.65±0.34	6.69±2.85	36.17±5.02	50.13±13.14	3.13±1.14	6.10±2.15	49.02±8.25	67.15±8.47	259.64±40.85	305.86±39.64
t	0.745	3.182	0.495	13.70	1.295	4.494	0.650	7.961	1.002	6.142	0.580	4.386
P	0.457	0.002	0.621	<0.001	0.197	<0.001	0.517	<0.001	0.312	<0.001	0.563	<0.001

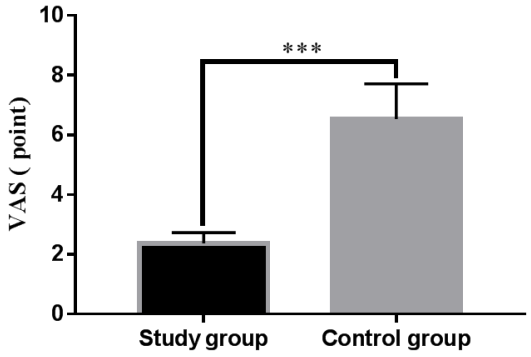

Figure 2. Comparison of VAS scores between the two groups.

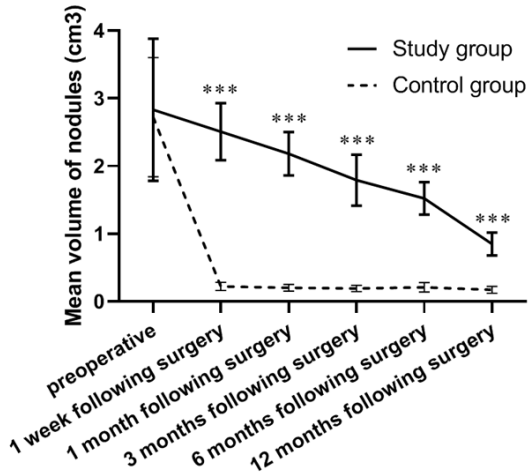

Figure 3. Mean volume of nodules with time.

(8.46±2.32) d and (6.84±2.44) d, and the hospital stay of the study group and control group was (14.14±3.18) d and (11.82±2.83) d. The functional recovery time and hospitalization time were significantly shorter in the study group compared with the control group (P< 0.001) **Table 7**.

Comparison of postoperative complications, cosmetic score, and symptom score

The study group yielded a significantly lower postoperative complication rate than the control group (4.00% vs. 14.00%, P<0.05), as shown in **Table 8**. In the study group, the cosmetic score was (89.25±11.25) while the symptom score was (8.26±1.86); In the control group, the cosmetic score was (80.16±9.27) while the symptom score was (15.15±3.24). The cosmetic score was higher and the symptom score was lower in the study group compared with the control group (both P<0.05) **Table 9**.

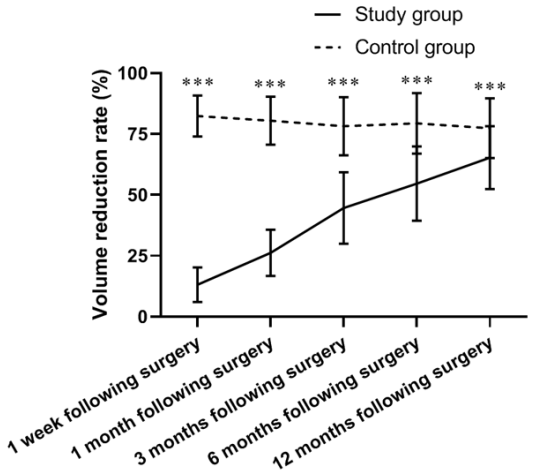

Figure 4. Volume reduction rate with time.

Discussion

Thermal ablation technology is currently one of the commonly used minimally invasive treatment techniques in clinical practice, including radiofrequency ablation, laser ablation, and microwave ablation, which is based on thermal degeneration and coagulative necrosis of diseased cells by heating [16]; and subsequently, the necrotic tissue will gradually be absorbed by the body, thus playing the role of local lesion inactivation [17]. Benign thyroid nodule is a common clinical disease. Due to the rather hidden clinical manifestations of benign thyroid nodules in the early stage, patients are usually diagnosed after obvious discomfort or the presence of pathologic appearance, which often requires surgical treatment [18]. Although the effect of current small incision surgery on the appearance of the patients has been improved to a certain extent, it still causes great trauma to patients [19].

It has been reported that ultrasound-guided microwave ablation fails to successfully shrink the nodules [20]. Accordingly, it is essential to explore the relevant factors with predictive value for efficacy [21]. The results showed significant differences in WBC, VAS score, and the levels of hs-CRP, TNF-α, and IL-6 between the two groups; In the acute stage of trauma, monocytes, lymphocytes, and endothelial cells

Table 6. Thyroid function indexes of patients in the two groups

Group	n	TSH (mU/L)	FT3 (nmol/L)	FT4 (nmol/L)	TT4 (nmol/L)
Study group	75	5.02±0.84	2.46±0.32	88.39±11.36	91.39±14.63
Control group	75	8.39±1.35	1.84±0.44	66.39±9.25	73.25±11.25
t		18.36	9.87	13.01	8.51
P		<0.001	<0.001	<0.001	<0.001

Table 7. Functional recovery time and hospitalization time in the two groups

Group	n	Recovery time of thyroid biochemical indexes	Hospitalization time
Study group	75	8.46±2.32	14.14±3.18
Control group	75	6.84±2.44	11.82±2.83
t		4.167	4.720
P		<0.001	<0.001

Table 8. Postoperative complications in the two groups

Group	N	Nausea	Hoarseness	Wound infection	Neck hematoma	Complication rate [n (%)]
Study group	75	1	1	1	0	3 (4.00)
Control group	75	3	4	2	1	10 (13.33)
χ^2						4.284
P						0.016

Table 9. Cosmetic score and symptom score of patients in the two groups

Group	n	Cosmetic score	Symptom score
Study group	75	89.25±11.25	8.26±1.86
Control group	75	80.16±9.27	15.15±3.24
t		5.749	17.00
P		<0.001	<0.001

secrete IL-6 in large quantities, leading to a significant increase in the level of serum IL-6 [22] and inducing the production of CRP by hepatocytes. N and NE are the most common indicators of the stress response. Currently, it has been confirmed that the changes in cytokine levels in the body after surgery are closely related to the size of the wound. Relevant studies also pointed out the involvement of IL-6 in the early postoperative inflammatory response [23]. The levels of IL-6, N, and NE rise rapidly after surgery, and the greater the degree of surgical trauma, the higher the levels of IL-6, N, and NE [24]. Moreover, traditional surgical treatment cannot guarantee complete resection of the nodules, given the existence of multiple nodules in many cases. As a consequence, the surgical trauma caused by traditional surgical treatment gives rise to relatively large physical damage to patients and significantly increases the risk of postoperative infections. By contrast, the use of ultrasound-guided microwave ablation to treat patients with benign thyroid nodules contributes to less intraoperative blood loss, shortened duration of operation and hospital stay, fewer complications, and better quality of life scores. The position of the recurrent laryngeal nerve may experience changes due to the uplift of the greater thyroid nodule or neuroanatomical variation, resulting in a closer distance between the recurrent laryngeal nerve and the thyroid nodule. Ultrasound-guided microwave ablation can realize real-time monitoring of the “dangerous triangle” where the recurrent laryngeal nerve is located, which can effectively avoid damage to the recurrent laryngeal nerve and reduce the incidence of postoperative complications. The efficacy and safety of ultrasound-guided microwave ablation for benign thyroid nodules have been confirmed by numerous studies, which pointed out a reduction rate of the volume of thyroid nodules of 82%-95%. Similar results have been obtained in this study, indicating a promising therapeutic effect of the ultrasound-guided microwave ablation on the reduction of benign thyroid nodules.

Notwithstanding positive clinical results, endoscopic thyroidectomy is associated with surgical wounds and postoperative complications due to long operation time, large dissection surface, and severe postoperative pain. Ultrason-guided percutaneous microwave ablation of thyroid nodules is a minimally invasive technique that involves the coagulation and necrosis of target tissue cells by heating, which has gradually become a research hotspot and trend of minimally invasive treatment of

thyroid diseases [25]. Anesthesia, surgery and emotional stress could induce stress response. In clinical practice, the level of stress hormones and the changes of immune factors are often adopted to comprehensively evaluate the degree of stress response of the patients. The stress response could stimulate the hypothalamic-pituitary-adrenocortical axis, enhance the function of the anterior pituitary-adrenocortical, and release a large amount of adrenocorticotropin from the anterior pituitary. Ultrasound-guided percutaneous microwave ablation is used to determine the degree of traumatic stress of the patient. After operation, WBC and the levels of TNF-α, hs-CRP, IL-6, E, and NE in the two groups increased significantly but lower in study group ($P<0.05$), which is consistent with results of previous studies, suggesting predominant mitigation of the patient's stress response and better postoperative recovery [26]. The mean volume of nodules decreased significantly with time, indicating the effectiveness and safety of ultrasound-guided microwave ablation for the treatment of benign thyroid nodules. The serum levels of TSH, FT3, FT4, and TT4 of the study group were better than the control group ($P< 0.05$), indicating that ultrasound-guided percutaneous microwave ablation is effective in determining the lesion and causes less damage to the patient's thyroid function [27]. In addition, the cosmetic score was higher and the VAS and symptom scores were lower in the study group compared with the control group (all $P<0.05$). It indicates that this procedure has high safety and can alleviate the degree of postoperative pain and reduce the impact on the surrounding tissues and nerves of the thyroid gland, thereby reducing the incidence of postoperative throat reflux symptoms and the degree of voice disturbance. The cosmetic satisfaction score of the observation group was significantly higher than that of the control group. The scar of microwave ablation is the same as the neck crease, because in addition to minimizing postoperative scarring, ultrasound-guided percutaneous microwave ablation applied absorbable sutures with small cuts during the suture process, which can reduce the surgical scars.

Development of high-frequency ultrasound technology has allowed new breakthroughs in thyroid surgery. This study provides more evidence-based medical references for ultrasound-guided microwave ablation of benign thyroid nodules. The limitation of this study lies in the absence of long-term follow-up, which will be conducted in future studies to observe further treatment effects.

In summary, in patients with benign thyroid nodules, the ultrasound-guided microwave ablation could effectively reduce nodule volume, preserve thyroid function, and improve the quality of patients' daily life, which is closely related to reduced inflammatory responses.

Disclosure of conflict of interest

None.

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