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A comparison of the 2 thermal ablation procedures for the management of benign thyroid nodules

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Abstract

Introduction: In recent years, ultrasound (US)-guided thermal ablation techniques have come to the fore as minimally invasive alternatives to surgery. The purpose of this study was to assess the effectiveness and safety of radiofrequency ablation or microwave ablation procedures in patients with benign thyroid nodules.

Material and methods: This retrospective and single-centre study consisted of 55 patients and 62 benign thyroid nodules that were treated either with radiofrequency ablation (RFA) or microwave ablation (MWA) in our hospital between January 2020 and March 2022. All the patients were at high risk for surgery or with symptomatic TNs and who refused surgery. The TNs diagnosed as benign from the fine-needle aspiration biopsy were evaluated in terms of volume reduction, symptom, and cosmetic scores. In addition, these 2 treatment modalities were compared to each other.

Results: Out of 55 patients, 44 (80%) were female and were aged between 24 and 97 years with a median age of 50 years. RFA was applied to 54.5% (n = 30) of the participants, and MWA was applied to 46.5% (n = 25). The volume reduction rate (VRR) after RFA and MWA at the first month was 63.4 ± 14.2 and 65.7 ± 13, respectively. No significant difference was detected between the 2 groups in terms of VRR (p = 0.51). In addition, the mean symptom and cosmetic scores decreased significantly in both procedures, and there was a significant difference due to the symptom score change in the RFA group compared to the MWA group. Of all the patients, one patient experienced haematoma in the RFA, and one patient had transient voice change in the MWA group. No life-threatening complications were noted.

Conclusion: In the treatment of benign symptomatic thyroid nodules, both RFA and MWA are options worthy of consideration in terms of efficacy and safety.

Key words: *benign thyroid nodules; radiofrequency ablation; microwave ablation; volume reduction rate; symptom and cosmetic scores*

Introduction

Thyroid nodules (TNs) are a common clinical issue. The diagnosis of thyroid incidentalomas occurs more commonly in high-income countries, where imaging is increasingly used, preferably for patients with access to medical care [1]. In general, 50% of TNs are detected with ultrasonography (USG); however, the prevalence decreases roughly to 5% due to the physical examination [2, 3]. TNs are approximately 4 times more common in women and their prevalence increases depending on various factors like age and iodine deficiency [3].

At present, surgery is still the main treatment method for thyroid nodules. However, surgery has some drawbacks such as hoarseness, laryngeal nerve injury, scar development due to the wound healing, the risk of hypothyroidism, and iatrogenic hypoparathyroidism. In addition, surgery performed under general anaesthesia and requires hospitalization [4]. Moreover, ablation therapies are less costly than surgery [5]. Therefore, less invasive treatment methods such as chemical ablation and thermal ablation are gaining popularity, and image-guided ablation has been recommended by many guidelines and consensus statements in the treatment of benign TNs [4–8].

In this study, some clinical and functional outcomes were evaluated using radiofrequency ablation (RFA) and microwave ablation (MWA) treatment methods in cytology-confirmed benign TNs. The primary aim

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of this study was to evaluate the reduction rates of thyroid nodules at one month after RFA and MWA procedures, and whether there is a significant difference in volume reduction between these 2 groups. The secondary aim was to evaluate the rate of change in symptom and cosmetic scores during follow-up and the rate of complications that occur with these 2 techniques.

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Material and methods

This retrospective study was started after necessary permissions were obtained from the Ethics Committee of Health Sciences University Istanbul Kanuni Sultan Suleyman Training and Research Hospital with the reference number 2022.03.74.

The study had a retrospective design and was conducted among patients who applied to the Endocrinology and Metabolism Diseases and Geriatrics outpatient clinics during the period from January 2020 to March 2022. Written informed consent was obtained from all patients following a detailed explanation of the procedure and the complications (pain, haematoma, infection, burn, hoarseness, hypothyroidism, etc.) that may occur due to it. The protocol of the study was conducted in accordance with the ethical principles stated in the "Declaration of Helsinki".

Patients aged over 18 years, diagnosed with USG-guided fine-needle aspiration biopsy (FNAB) as benign thyroid nodules by pathologists trained in this subject, who had compression symptoms or cosmetic problems, and patients refusing surgery or at high risk for surgery were included. The criteria for exclusion from the study were age below 18 years, having a diagnosis of pure cystic nodule or combination of solid-cystic nodules (< 25% of solid component) on USG imaging, known history of radiotherapy to neck, presence of coagulation disorders, and patients with missing data or who did not continue follow-up.

Patients with symptomatic benign thyroid nodules referred from endocrinology, geriatrics, and internal medicine outpatient clinics were evaluated by the same endocrinologist preoperatively, and their postoperative first-month controls were performed by 2 different endocrinologists. Interventional procedures were applied to each patient by the same interventional radiologist.

Pure cystic nodules were not treated, and solid or mixed (minimum 70% solid component) nodules were taken when selecting the patient.

Haemogram, coagulation, and thyroid function tests were recorded before and after the first month of the ablation therapy.

In addition to laboratory assessment, the symptom scores and the cosmetic score were determined. The symptom scores (neck pain, dysphasia, foreign body sensation, discomfort, and cough) were self-measured by patients using a 10 cm Visual Analogue Scale (grade 0–10). Also, the cosmetic score was evaluated by the physician as follows [8, 9]:

— no palpable nodule;
— no cosmetic problem but palpable nodule;
— a cosmetic problem with swallowing only;
— easily observable cosmetic problem.

The features of the nodules such as size, shape, calcification status, and solid/cystic ratio were evaluated with the help of USG before the ablation. Biopsies were taken from thyroid nodules for control purposes, nodules with cystic contents were aspirated and cytological sampling was performed. Biopsies were reported cytopathologically by using the Bethesda classification (10). Additionally, volumetric measurements of the nodules were made using the formula $V = \varpi abc/6$ (a = largest diameter, b and c = other vertical diameters in millimetres).

The treatment of the patients under anticoagulant treatment was stopped 7 days before the intervention, and the coagulation test results were checked before the ablation treatment.

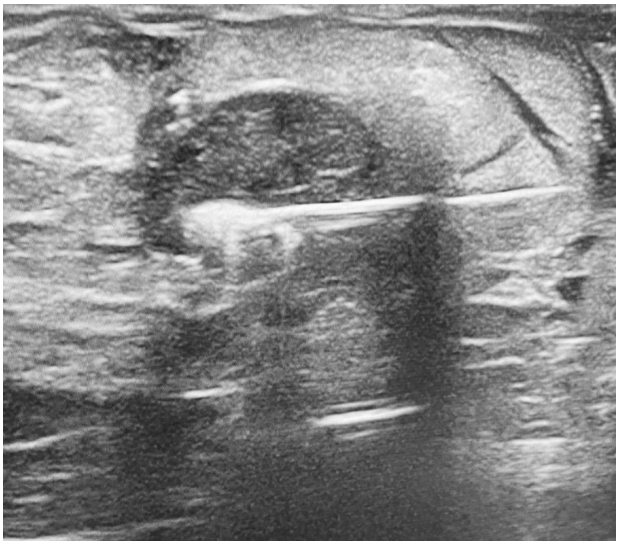

Figure 1. *During the procedure, multiple echogenic microbubbles (arrow) around the antenna tip were noted*

Radiofrequency ablation procedure

This procedure was performed for all patients under local anaesthesia. An electrode (18 g thickness, length 100 mm, active burning tip 3 mm) with an internal cooling system and RF generator were used during the intervention (Apro, Gyeonggi, Korea). The energy was distributed effectively, and tissue carbonization was prevented with the help of a cooling system that circulated physiological saline with the help of a pump through the electrode. Local anaesthesia was applied in line with the localization of the nodule. Important anatomical neighbourhoods were dissected and removed with 5% dextrose. The electrode was placed in the posterio-inferior part of the nodule and ablation was started with the "moving shot technique" (Fig. 1).

The initial ablation energy power of the system operating between 40 and 100 W was set to 25 W, and the electrode was moved to other parts of the nodule when a hyperechoic region was observed in the nodule 20–45 seconds after the ablation. If the hyperechoic zone was not seen after 45 seconds, the energy power was increased in 5-W steps up to a 60-W limit. The procedure was terminated after all regions were visualized as hyperechoic. The patient was kept under observation for approximately one hour after the procedure, controls were made, oral analgesics were prescribed, and the patient was discharged to be called for follow-ups.

Microwave ablation procedure

The MWA method was also performed with similar principles. The system consisted of a generator working at microwave frequency and producing power at a wavelength of 2.45 GHz, and probes working depending on this (ECO, Nanjing, China). The generator can produce microwave energy in the power range 60–140 W and send it continuously from 10 seconds to 6 minutes without losing the energy produced. High temperatures can be controlled because the probes have a temperature control. For this reason, it is ensured that the probes are in contact with the liquid. MWA probes can ablate 1–6-cm nodules in a single procedure (Fig. 2).

In line with the localization of the nodule, a 2-mm skin incision was made under local anaesthesia and the MWA probe was placed in the posterior part of the nodule to be processed under USG. Transisthmic interference was preferred to see the entire length of the microwave probe and to preserve neurovascular structures. The ablation was continued by advancing the MWA probe towards the other parts of the nodule because the appearance of hyperechogenic areas on USG images during MWA indicates

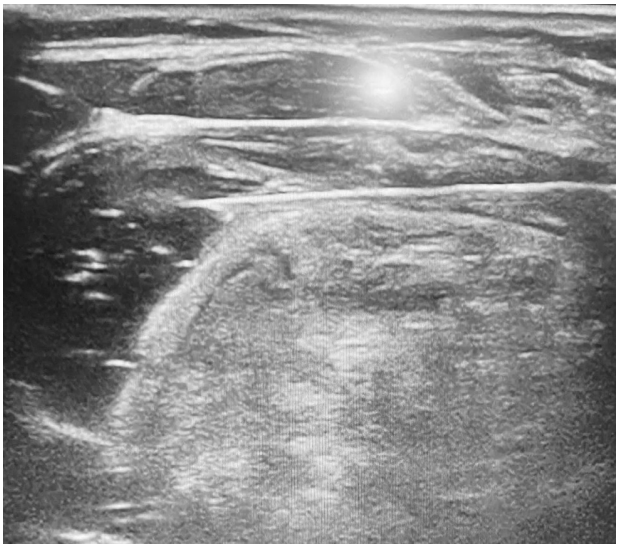

Figure 2. *Carotid was removed from the nodule by hydro-dissection technique*

the formation of heat in the ablation area. The patient was kept under observation for approximately one hour after the procedure, oral analgesics were prescribed, and the patient was discharged to be called for follow-ups.

Statistical analysis

Statistical analyses were made using SPSS version 22 software. The conformity of the variables to the normal distribution was evaluated with analytical (Kolmogorov-Smirnov) and visual (histogram and probability graphs) methods. Descriptive analyses were given by using the mean ± standard deviation (SD) for normally distributed variables and median (minimum-maximum) for non-normally distributed variables. Because the basal thyroid nodule volume measured before the procedure and the cosmetic score calculated one month after the procedure were not normally distributed, comparisons were made by using the Wilcoxon signed rank test. A comparison of the scores was made using Student's t-test for dependent groups because the compression symptom score, which was evaluated before and one month after the intervention, was normally distributed. The cases in which the *p*-value was below 0.05 were considered statistically significant.

Results

The study sample consisted of 55 patients. Forty-four (80%) were female, 11 (20%) were male, and they were aged between 24 and 97 years with a median age of 50 years. More than one nodule underwent intervention in some patients. The total number of treated nodules was 62. Radiofrequency ablation was applied to 54.5% (n = 30) of the participants, and MWA was applied to 46.5% (n = 25). The baseline characteristics of the participants are given in Table 1.

Table 1. *The baseline features of the participants*

Parameters	Results
Age [years]	50 (24–97)
Gender	
Female	44 (80%)
Male	11 (20%)
Free T4 [ng/dL]	1.1 ± 0.2
TSH [μIU/L]	0.99 ± 0.76
Thyroid nodule volume [mL]	15 (0.4–459)
Symptom score	7.2 ± 1.7
Cosmetic score	3.3 ± 0.8

TSH — thyroid-stimulating hormone; T4 — thyroxine

The comparison of the nodule volumes, symptom, and cosmetic scores of all patients before and after the treatment modalities are shown in Table 2.

The median pre-treatment nodule volume decreased statistically significantly from 15 mL to 4.8 mL ($p < 0.001$) with a mean VRR of 64.6 ± 13.6 % at one-month follow-up. Patients also achieved significant improvement in the cosmetic and symptom scores after both thermal ablation techniques ($p < 0.001$).

The patients were treated with 2 different methods: radiofrequency ablation and microwave ablation. The comparison of the baseline and first-month results of the patients in the RFA or MWA groups are given in Table 3.

In the RFA group, the median initial nodule volume was 16.35 mL, and it significantly decreased to 5.4 mL one month after treatment ($p < 0.001$). The mean symptom score was 7.5 ± 1.8, and we observed a statistically significant improvement (2.7 ± 1.3) at the one-month follow-up ($p < 0.001$). The median cosmetic score was 4 (ranged from 2 to 4) before the procedure, and this score reduced significantly to a median of 2 (ranged from 1 to 2) after RFA ($p < 0.001$).

Table 2. *Baseline and first-month measurements of the patients who underwent both procedures*

	Baseline	1st month	p-value
Nodule volume [mL]	15 (0.4–459)	4.8 (0.18–192)	< 0.001[a]
VRR		64.6 ± 13.6	
Symptom score	7.2 ± 1.7	2.8 ± 1.1	< 0.001[b]
Cosmetic score	4 (14)	1 (1–3)	< 0.001[a]

[a]Wilcoxon signed rank test; [b]Student's t-test; VRR — volume reduction rate

Table 3. *Comparison of the results before and after the first month in each group*

	Baseline	1st month	p-value
RFA			
Nodule volume [mL]	16.35 (0.67–459.8)	5.4 (0.18–192)	< 0.001
Symptom score	7.5 ± 1.8	2.7 ± 1.3	< 0.001
Cosmetic score	4 (2–4)	2 (1–2)	< 0.001
MWA			
Nodule volume [mL]	14 (0.4–75.3)	4 (0.19–16.4)	< 0.001
Symptom score	6.9 ± 1.6	2.8 ± 1.09	< 0.001
Cosmetic score	3 (1–4)	1 (1–3)	< 0.001

RFA — radiofrequency ablation; MWA — microwave ablation

In the MWA group, there was statistically significant nodule volume reduction from 14 mL to 4 mL ($p < 0.001$) after one month. The mean symptom score also significantly decreased from 6.9 ± 1.6 to 2.8 ± 1.09 ($p < 0.001$). The median cosmetic score was 3 (ranged from 1 to 4) before MWA, and it improved significantly to a median of 1 (ranged from 1 to 3) at the one-month follow-up ($p < 0.001$).

The comparison between RFA and MWA procedures with respect to the VRR and symptom and cosmetic score changes are presented in Table 4 and Table 5, respectively.

The volume reduction rate (VRR) after RFA and MWA at the first month was 63.4 ± 14.2 and 65.7 ± 13, respectively. No significant difference was noted between the 2 groups in terms of VRR ($p = 0.51$). There was also no significant difference with respect to cosmetic score change ($p = 0.098$) but the symptom score change was significantly higher in RFA group compared to the MWA group ($p = 0.019$).

When the side effects and complications were evaluated, it was found that 7 patients had pain (4 in the RFA group, 3 in the MWA group). The pain was relieved with simple analgesics within a few days. No significant difference was found between the 2 groups in terms of pain ($p = 0.62$). Of all the patients, one patient experienced haematoma in the RFA group and one patient had transient voice change in the MWA group. No skin burn, Horner's syndrome, nodule rupture, or tracheal and oesophageal damage were observed.

Discussion

Thyroid nodules are one of the most common endocrinological disorder seen in clinical practice. Their incidence is increasing with the frequent use of ultrasonography in clinical practice, and their prevalence is reported to vary between 20% and 70% [11]. A total of 85–93% of thyroid nodules are benign and do not require treatment. However, the patient may require

Table 4. *The comparison between the 2 treatment modalities due to the volume reduction rate*

	Baseline volume	1st-month volume	p-value
RFA	16.35 (0.67–459.8)	5.4 (0.18–192)	0.51
VRR		63.4 ± 14.2	
MWA	14 (0.4–75.3)	4 (0.19–16.4)	
VRR		65.7±13	

RFA — radiofrequency ablation; MWA — microwave ablation; VRR — volume reduction rate

Table 5. *Comparison between the 2 treatment modalities in terms of symptom and cosmetic score changes*

	RFA	MWA	p-value
Symptom score change	5 (0–8)	4 (2–10)	0.019
Cosmetic score change	2 (1–3)	2 (0–3)	0.098

RFA — radiofrequency ablation; MWA — microwave ablation

treatment if the nodules are likely to be malignant or have symptoms related to nodule compression such as neck pain, dysphagia, foreign body sensation, and cough, or if they cause cosmetic problems [4]. Although the main treatment of thyroid nodules is surgery, less invasive treatment methods are starting to be preferred because of the complications of surgery. USG-guided thermal ablation (TA) techniques have come to the fore as minimally invasive alternatives to surgery for those at high risk for surgery or for patients with symptomatic benign TNs who refuse surgery. These consist of radiofrequency ablation (RFA), laser ablation treatment (LAT), microwave ablation (MWA), and high-intensity focused ultrasound (HIFU) [10, 11].

It has been shown in previous studies that RFA is a successful alternative to surgery in the treatment of benign TNs. The reduction in nodule volume has been reported to range from 33 to 58% at one month after RFA [9]. In a study of Escobedo et al., the rate of volume reduction in the first month was found to be 34.2 ± 17.2% [14]. In another retrospective study including 119 patients, Bisceglia et al. determined a median nodule volume reduction rate of 47.10%, ranging from 31.30 to 56.50 % one month after RFA [12]. In our study, the mean nodule volume reduction was 63.4% after one-month follow-up.

Microwave ablation (MWA), on the other hand, is a newer thermal ablation method used after RFA in the treatment of thyroid nodules [13]. It has advantages such as larger ablation volume, higher and more homogeneous heat distribution, and faster ablation time compared to RFA [14]. In the study of Zhi et al., a 72% reduction was observed in nodule volume at the end of the 3rd month with MWA [15]. Luo et al. used MWA on 180 benign TNs of 171 patients and followed these patients for 3 years. Nodule volume decreased by 47.1% in the first month and by 68.2% in the third month, and by 93.2% in the third year [16]. In the previous study, the mean nodule volume reduction was 65.7 % in the first month after the MWA procedure.

In studies comparing the efficacy of RFA and MWA, generally both techniques were found to be similarly effective. One of the first studies about this subject was designed by Yue et al. In this study, the data of 260 patients with benign TNs were retrospectively reviewed for comparison of RFA and MWA procedures. Among these patients, 158 patients underwent MWA and 102 patients underwent RFA. At the end of the 1st and 6th month, the reduction rates in the thyroid nodule volume were 24.0 ± 5.9% and 79.4 ± 8.6% in the RFA, and 22.3 ± 9.1% and 77.2 ± 10.8% in the MWA group, respectively. Although the rate of nodule volume reduction was found to be higher in the RFA group, there was no statistically significant difference between these 2 ablation techniques at 6 months. In addition, no significant differences were noted due to the cosmetic and symptom scores, but a significant improvement was found compared to the pre-treatment scores [17]. Javadov et al. conducted a prospective study to evaluate the clinical and functional results of RFA and MWA treatments on benign TNs. In this study, 50 MWAs and 50 RFAs with benign TNs were evaluated between 2014 and 2017. As a result, VRR after RFA at the 1, 3, and 6 month after RFA was 42%, 56%, and 65%, respectively, and 46%, 64%, and 68%, after MWA. They concluded that VRRs achieved by RFA or MWA at 1, 3, and 6 months of follow-up were not statistically significant, like as the cosmetic and symptom scores of the patients [18]. In a prospective study in which Cheng et al. compared the effectiveness of RFA and MWA in 1252 patients and a total of 8 centres including 1351 nodules, no significant differences were detected between the 2 procedures in terms of volume reduction at the 3-month follow-up. However, it was found that the results were significantly better in the RFA group in the 6th and 12th months [19]. Consistent with the literature data, our study demonstrates that one procedure was not found to be superior to the other with respect to the volume reduction. Significant improvement was observed in the symptom and cosmetic scores after both procedures. However, the reduction in the symptom score was significantly higher in the RFA group compared to the MWA group. Larger initial nodule size in the RFA group may result in higher symptom scores. This finding could be explained by the fact that a larger initial size in the RFA group may increase the symptom score. Therefore, it may cause them to feel better in their complaints after the procedure.

The safety of both procedures has been demonstrated in many studies. The complication rate varies depending on factors such as the operator's experience (trained operators to perform the procedure), the number of cases included in the study, and maybe the type of technique performed. In a multicentre prospective study that we previously mentioned, major postoperative complications developed in 71 cases, including voice changes in 64 cases, nodule ruptures in 6 cases, and Horner's Syndrome in one case [19]. In the study that was conducted by Hussain et al., self-limiting local bleeding was observed in one patient and a temporary voice change was observed in one patient, which resolved in 6 months [20]. The authors considered transient voice change as a minor complication. In another study, transient voice change after RFA lasting for one hour was also evaluated as a minor complication [21]. Of all the patients, one patient experienced haematoma in the RFA group, and one patient had transient voice change in the MWA group

and recovered in less than one hour after a cold 5% dextrose injection. The prevailing opinion in the literature is that voice change is a major complication and is mostly due to the nerve damage. However, haemorrhage or temperature increase due to thermal conduction may also cause voice change. Because the voice change resolved in a short time and did not require treatment except cold 5% dextrose injection, we thought that it was not due to nerve damage, and we did not consider it as a major complication.

The main limitations of urrentt study were the relatively small sample size and the short follow-up period. Most of the studies about this subject in the literature are retrospective, similarly to our study. We think that more prospective randomized studies comparing these two techniques are needed.

Conclusion

Both RFA and MWA are options worthy of consideration with respect to efficacy and safety in the treatment of benign, symptomatic thyroid nodules, In our country, thyroid nodule is detected in approximately one of every 3–4 people. For this reason, new alternative therapies should be considered in the management of thyroid nodules due to their high prevalence. We think that awareness of thermal ablation methods should be increased in selected patients due to the drawbacks, need for hospitalization, risk of anaesthesia, life-long L-thyroxine replacement therapy, and therefore economic burden of surgery.

Conflicts of interest

All authors have no conflicts of interest to declare with respect to the research and publication of this article.

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