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Comparison of Volumetric and Cosmetic Scoring Changes After Treatment of Benign Thyroid Nodules Using Microwave Ablation and Ethanol Ablation Therapy

Mikrodalga Ablasyon ve Etanol Ablasyon Tedavisi Uygulanan Benign Tiroid Nodüllerinin Tedaviden Sonra Hacimsel ve Kozmetik Skorlama Değişikliklerinin Karşılaştırması

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ABSTRACT

Aim: This study retrospectively evaluated the effects of treatment of benign mixed-type and spongy-type thyroid nodules with microwave ablation (MWA) and ethanol ablation (EA) therapies. The changes in volume obtained by ultrasonography and cosmetic scores were examined. The efficiency of both treatment methods was also compared by statistical analyses.
Methods: Between July 2015 and July 2020, archive scanning was performed for patients who underwent MWA and EA in the radiology clinic. As a result, 57 MWA and 55 EA patients were included in the study. Nodule volumes from before the treatment, 3 months, and 6 months after ablation treatment were noted for each case. Cosmetic scores for all patients were also examined.
Results: A statistically significant difference was found in the mean nodule volume at 6 months between MWA and EA, with MWA being more successful ($p<0.05$). The MWA technique also resulted in significantly higher mean cosmetic score reduction ($p<0.05$).
Conclusion: Minimally invasive approaches are increasingly adopted in the treatment of benign thyroid nodules, and both MWA and EA are effective and safe treatments techniques. The results show that MWA treatment leads to better cosmetic scores and nodule volume changes in patients with benign mixed-type and spongy-type thyroid nodules.

Keywords: Thyroid nodule, microwave ablation, ethanol ablation, ultrasound, cosmetic score

ÖZ

Amaç: Bu çalışma geriye dönük olarak benign mikst-tip ve süngerimsi-tip tiroid nodüllerinin mikrodalga ablasyon (MWA) ve etanol ablasyon (EA) terapileri ve tedavi etkinliğini değerlendirmiştir. Ultrasonografi ve kozmetik skorlarla elde edilen hacim değişiklikleri incelendi. Her iki tedavi yönteminin etkinliği de istatistiksel analizlerle karşılaştırıldı.
Yöntem: Temmuz 2015 ile Temmuz 2020 tarihleri arasında radyoloji kliniğinde MWA ve EA yapılan hastalara arşiv taraması yapıldı. Sonuç olarak 57 MWA ve 55 EA hastası çalışmaya dahil edildi. Her vaka için tedavi öncesi, ablasyon tedavisinden 3 ay ve 6 ay sonraki nodül hacimleri not edildi. Tüm hastalar için kozmetik skorlar da incelendi. **Bulgular:** MWA ile EA arasında 6. ayda ortalama nodül hacminde istatistiksel olarak anlamlı bir fark bulunmuş olup, MWA daha başarılıydı ($p<0.05$). Ayrıca MWA tekniği, anlamlı olarak daha yüksek ortalama kozmetik skor azalmasıyla sonuçlanmıştır ($p<0.05$).
Sonuç: Minimal invaziv yaklaşımlar, benign tiroid nodüllerinin tedavisinde gider-ek daha fazla benimsenmektedir ve hem MWA hem de EA etkili ve güvenli teda-vi teknikleridir. Sonuçlar, MWA tedavisinin benign mikst-tip ve süngerimsi-tip tiroid nodülleri olan hastalarda daha iyi kozmetik skorlara ve nodül hacim değişikliğine yol açtığını göstermektedir.

Anahtar kelimeler: Tiroid nodülü, mikrodalga ablasyon, etanol ablasyon, ultrason, kozmetik skor

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INTRODUCTION

Thyroid nodules are mostly benign lesions that are quite common in a routine examination. Clinically, palpable nodules are found in 5-10% of the population, and there is a lifetime possibility of developing new thyroid nodules in 10% of patients [1,2]. The possibility of detecting nodules in the thyroid gland increases with age, and they are more common in females than males [3]. Nodules that cannot be palpated by physical examination are more likely to be detected by ultrasonography (USG), and the probability of encountering nodules in ultrasound examinations performed for screening purposes may exceed 50%. The widespread use of ultrasound imaging in daily practice has led to more detection of asymptomatic nodules [4,5].

Treatment is required for nodules that cause pressure on the respiratory tract and esophagus and cause a feeling of tension [6,7]. Although surgery is the main treatment method, aspiration can be applied for cystic thyroid nodules [8,9]. Minimally invasive approaches have been used more frequently in the treatment of benign mixed-type and spongy-type nodules in recent years, and ethanol ablation (EA) therapy can be easily performed [10,11]. Alternatively, microwave ablation (MWA) therapy is a relatively new minimally invasive treatment method that can significantly reduce the volumes of nodules [12]. MWA is widely used in the treatment of lung, liver, and kidney tumors, and its most important advantage is that it is less painful [13,14].

Mixed-type solid-component cystic nodules and spongy-type thyroid nodules are proven to be benign by fine-needle aspiration biopsies (FNAB). Ethanol is injected into the cyst, and ablation is performed on the nodule in these cases (Figure 1) [15-18]. In MWA therapy, a thin linear probe is inserted into the nodule with to reduce the nodule size and volume by using microwave energy [19]. In the follow-up of benign thyroid nodules, the volume changes are monitored with ultrasound, and the simple and very useful WHO cosmetic scoring system is applied before and after ablation treatment. The score's range is from 1 to 4 (1, no palpable mass; 2, no cosmetic problems, but palpable mass; 3, the mass only causes swallowing difficulties and is visible at close range; 4, the mass is easily visible). Accordingly, for scores ≥ 2, the choice of ablation treatment can be made by evaluating other accompanying symptoms [19,20].

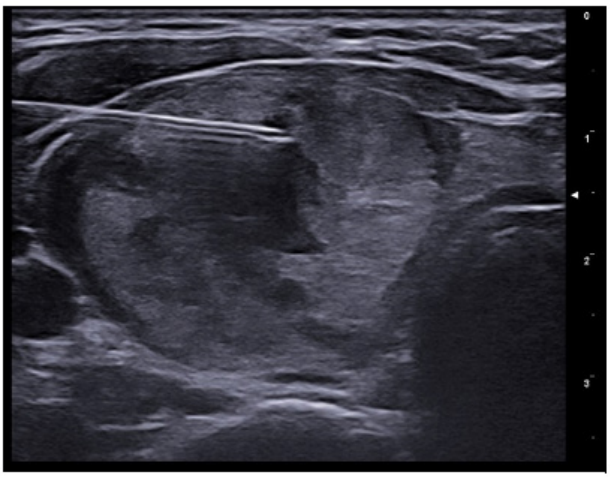

Figure 1. Ultrasound image showing a fine-needle inserted at the beginning of ethanol ablation treatment in a spongy-type nodule located in the right lobe of the thyroid gland.

With both ablation methods, the duration of hospital stay and the complications that may arise from surgery can be minimized [20,21]. In this study, the volumes obtained and changes in cosmetic scores after MWA and EA were evaluated retrospectively. In addition, a statistical analysis of the results was done to compare the efficiency of both treatment methods.

MATERIAL AND METHOD

This retrospective study was approved by the University of Health Sciences institutional review board (IRB protocol number: 20/347). Treatment methods were carried out according to approved guidelines. Written informed consent was obtained from all patients before biopsy and ablation procedures. Between July 2015 and July 2020, archive scanning was performed for patients who were proven to have benign with FNAB and underwent MWA and EA in the radiology clinic. The exclusion criteria were as follows: a history of chronic thyroiditis and thyroid gland surgery, a history of malignancy, the presence of congenital anomalies and pure cystic nodules, missing ultrasonographic data, BMI ≥35, and age under 18 years.

As a result, 57 MWA and 55 EA patients who

satisfied the eligibility criteria were identified and included in the study. Thyroid FNAB was performed before ablation therapies on the participants, and cosmetic scoring and USG data were also used to evaluate volumetric changes at the 3rd month and 6th month after treatment. In addition, the efficiency of MWA and EA was also compared.

B-mode ultrasound measurements of volume were performed by a radiologist who is experienced in USG and interventional radiology, and cosmetic scoring was performed for each patient in the same session. The volumetric measurements were performed using ultrasound images obtained in axial and sagittal planes by a 4–15-Mhz linear array probe (MyLab 9 eXP, Genova, Italy). EA and MWA procedures were applied in a single session.

No medication or contrast agents were administered during the ultrasound procedures at the 3rd and 6th month follow-up after the treatment. EA and MWA were performed on an outpatient basis, and patients were placed in a supine position with slight neck extension. They were followed-up throughout the day after the procedures were performed. Before the procedure, the location of the nodule was checked with ultrasound, and local anesthesia was applied under the skin with lidocaine. Ablation was performed under ultrasound guidance.

Statistical analysis

Statistical analysis of the data was performed using SPSS software (IBM SPSS ver. 22.0, IBM, Armonk, NY, USA). Descriptive statistics (median, frequency, percentage, minimum, maximum, mean, lowest, and highest) were used to express the central tendencies. Kolmogorov-Smirnov and Shapiro-Wilk tests were used to evaluate the normality of the quantitative data distributions. Correlations between parameters were tested using the Spearman correlation test. Pearson's chi-squared test was used to compare categorical variables. The Mann-Whitney U test was used to compare the differences between genders and laterality for data that were not normally distributed. The Kruskal-Wallis test was used to compare nodule volumes and cosmetic scores before the treatment and at the 3rd and 6th months. A p-value <0.05 was considered statistically significant.

RESULTS

A total of 112 patients participated in this study, including 36 males (32.1%) and 76 females (67.9%). The youngest case was a 20-year-old female, the oldest case was a 78-year-old male, and the median age was 49.00 years. Table 1 shows the detailed distribution of the cases by gender, mean age, and median age.

Table 1: Demographics

Gender	Male	Female	Total
n	36	76	112
Minimum age	33	20	20
Maximum age	78	74	78
Mean age	52.54	46.46	48.10
Median age	52.00	46.00	49.00
Std. deviation (±)	9.74	12.63	12.17

All patients had a single nodule, 57 patients (50.9%) received MWA, and 55 patients (49.1%) received EA in a single session. There were mixed-type nodules in 61 cases and spongy-type nodules in 51 cases. No statistically significant difference was found between genders and nodule types according to the chi-squared test of independence ($p>0.05$). There was no statistically significant difference between genders and ablation types. Similarly, when the nodule type and ablation procedures were compared, no statistically significant difference was found ($p>0.05$). The smallest subgroup was 5 males with spongy nodules, and the largest group was 21 females with mixed-type nodules, and both underwent EA. The distribution of nodule types by gender and ablation procedure is shown in Table 2.

Table 2: Distribution of nodule types by gender and ablation procedure

			Ablation procedure		Total
			EA (n)	MWA (n)	
Male	Nodule type	Mixed-type nodule (n)	11	11	22
		Spongious nodule (n)	5	9	14
	Total		16	20	36
Female	Nodule type	Mixed-type nodule (n)	21	18	39
		Spongious nodule (n)	18	19	37
	Total		39	37	76

In all patients who underwent MWA and EA, the mean nodule volume was 21.12 ml before

treatment, 5.96 ml at the 3rd month, and 3.78 ml at the 6th month. In cases with MWA, the mean nodule volume was 21.43 ml before treatment, 5.55 ml at the 3rd month, and 2.76 ml at the 6th month ($p<0.05$). In the EA group, the mean nodule volume was 20.86 ml at pretreatment, 6.34 ml at the 3rd month, and 4.71 ml at the 6th month ($p<0.05$).

After MWA, there was a reduction in the mean nodule volume of 74.1% at the 3rd month and 87.2% at the 6th month. After EA, there was a 69.6% reduction in mean nodule volume at the 3rd month and 77.5% at the 6th month. A statistically significant difference was found in mean nodule volume between MWA and EA groups at the 6th month ($p<0.05$). All patients who underwent MWA and EA had a decrease in mean nodule volume at the end of the 6th month, and no recurrence was detected.

Before ablation therapies, the lowest cosmetic score was 2, and the highest score was 4 among all patients. After ablation procedures, the lowest score was 1, and the highest score was 4 at the 3rd month, while at the 6th month, the lowest score was 1, and the highest score was 3. The mean cosmetic score at the 3rd month after MWA was 1.46±0.62, that after EA was 2.20±0.75, and the difference was statistically significant ($p<0.05$). Similarly, the mean cosmetic score was 1.20±0.40 at the 6th month for MWA and 1.64±0.66 at the 6th month after EA, and the difference was statistically significant ($p<0.05$). Table 3 shows the nodule volumes at pretreatment, the 3rd month, and the 6th month according to the ablation type, as well as the cosmetic scores. There was no statistically significant difference between genders, post-treatment cosmetic scores, and nodule volume changes. ($p>0.05$).

Transient partial loss of voice developed in 4 patients who underwent EA and 5 patients who underwent MWA, but it resolved spontaneously by the end of the second week. Pain and tingling radiating to the teeth and ears were present in 5 patients who underwent EA and 6 patients who underwent MWA, but they disappeared completely by the end of the 5th day. No skin burns, discoloration, subcutaneous infection, hematoma, or scarring developed after MWA or EA.

DISCUSSION

Benign thyroid nodules are lesions frequently encountered in clinical practice during a physical examination and various imaging procedures (mainly ultrasound). USG is an important non-invasive, inexpensive, easily accessible imaging method that is widely used in the detection and evaluation of thyroid nodules. It provides information about the nodule size and structure, as well as changes in the thyroid gland parenchyma [2-4]. Surgery is used as the main treatment method for benign thyroid nodules when compression occurs due to the mass effect of the nodule on the trachea and esophagus or when there is a significant feeling of tension in the skin [5-7]. Complications that may occur after surgery have led physicians to seek different methods for the treatment and management of thyroid nodules, and minimally invasive approaches are more frequently being used [9,16].

EA has been increasingly used in the treatment of benign thyroid nodules (mainly pure cystic nodules). In thyroid nodules that are proven to be benign with FNAB, ethanol is injected into the nodule, ablation is performed, and the sizes and volume of the nodule are reduced [6-11]. MWA is a relatively new minimally invasive treatment method that can be used effectively and safely on benign thyroid nodules. A reduction in size and volume is achieved by introducing microwave energy to the nodule through an ultrasound-guided thin linear probe during the procedure [12,13]. Both ablation techniques are very useful in minimizing the complications that may arise from surgery and make great contributions to shortening the length of hospital stay [19-21].

Kim et al. examined 20 cystic and 22 solid thyroid nodules, and ultrasounds were performed at 1 and 6 months after EA. At the 6th month, a 65% decrease in cystic nodule volume and 38.3% decrease in solid nodule volume were achieved, but the decrease in solid nodule volume was much less than in our study [10]. In our study, there was a 77.5% decrease in the mean volume of the mixed-type and spongy-type thyroid nodules in the 6th month ultrasound after EA.

Iñiguez-Ariza et al. examined EA in pure cystic and mixed-type nodules, and a reduction of more

Table 3: Nodule volumes and cosmetic scores before and after ablation therapies

Ablation procedure		n	Minimum	Maximum	Median	Mean	Std. deviation (±)
MWA	Pre volume	57	0.70	172.00	14.05	21.43	31.46
	3rd vol	57	0.05	23.00	3.75	5.55	5.38
	6th vol	57	0.01	13.10	1.70	2.76	2.99
	Pre cos	57	2	4	3	3.09	0.78
	3rd cos	57	1	3	1	1.46	0.62
	6th cos	57	1	2	1	1.20	0.40
EA	Pre volume	55	0.49	185.73	11.02	20.86	29.38
	3rd vol	55	0.2	44.56	3.24	6.34	8.62
	6th vol	55	0.07	16.58	2.90	4.71	4,39
	Pre cos	55	2	4	3	3.12	0.79
	3rd cos	55	1	4	2	2.20	0.75
	6th cos	55	1	3	2	1.64	0.66
Total	Pre volume	112	0.49	185.73	11.94	21.12	30.23
	3rd vol	112	0.2	44.56	3.67	5.96	7.23
	6th vol	112	0.01	16.58	2.12	3.78	3.89
	Pre cos	112	2	4	3	3.10	0.79
	3rd cos	112	1	4	2	1.84	0.78
		112	1	3	1	1.43	0.54

*Pre volume: Nodule volume before ablation, 3rd vol: 3rd month volume, 6th vol: 6th month volume

*Pre cos: Cosmetic score before ablation, 3rd cos: 3rd month score, 6th cos: 6th month score

than 50% was observed in both nodule types during the 2-year follow-up. They showed that EA can be a good alternative to surgery in mixed-type thyroid nodules [20]. Korkusuz et al. applied MWA to 18 solid thyroid nodules and achieved a reduction of more than 50% in the mean nodule volume by the 3-month follow-up [12]. In another study, they evaluated the efficacy of the treatment by functional scoring before and after MWA and obtained data supporting the effective use of MWA in the treatment of benign thyroid nodules [13].

Feng et al. performed MWA therapy on 11 patients using linear probes of different thicknesses and lengths and detected a nearly 50% reduction in benign thyroid nodule volumes at the 9th month. As a result, they stated that MWA can be a feasible method of treatment using linear microwave probes of different sizes and thickness according to the size and location of the nodule [14]. Yue et al. applied MWA to 222 patients and 477 benign thyroid nodules, which is the largest related case series known in the literature. The mean nodule volume was reduced by more than 50% in the 6th month after ablation, and they stated that MWA therapy can be used safely and effectively on benign thyroid nodules [19].

Although EA is routinely applied to cystic nodules, it was applied to spongy-type and mixed-type thyroid nodules in our study, unlike many other studies [8,11]. We could not find any study in the literature comparing the efficiency of MWA and EA performed on mixed-type and spongy-type thyroid nodules. Thus, the comparison of the effectiveness of these methods in this study stands out as an innovation. This study has one of the largest case series in the literature in terms of the total number of cases and the number of cases of MWA and EA in a single session [6,7,19]. When cosmetic scoring and volumetric changes were evaluated, there was a significant difference between MWA and EA, and MWA was more successful in the treatment of mixed-type and spongy-type thyroid nodules.

Limitations: One limitation in this study could be that the ablation procedure, post-treatment ultrasounds, and cosmetic scoring were performed by a single radiologist. As another limitation, there was relatively low number of male cases of spongy-type nodules undergoing EA compared to females, and follow-up for more than 6 months after ablation may also be conceivable [5]. In addition, there is a lack of studies comparing both ablation methods in mixed-type and spongy-type thyroid nodules to compare our data, which is another limitation. Our study shows that EA

can also be used in mixed-type and spongy-type nodules, but there is still a need for new studies with larger case series to compare both methods.

Conclusion: Minimally invasive approaches are increasingly being adopted in the treatment of benign thyroid nodules. Both MWA and EA are effective and safe minimally invasive treatment techniques for these nodules and are highly effective in reducing the length of hospital stay. Our study showed that MWA therapy is slightly more successful in improving the cosmetic score and nodule volume in these cases, but EA can also be used safely. With new research conducted with larger case series, the effectiveness of these techniques in such thyroid nodules can be confirmed, and indications for use will become more widespread.

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Ethics Committee Approval: University of Health Sciences institutional review board (IRB protocol number: 20/347).

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