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INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI: 10.21474/IJAR01/15410
DOI URL: http://dx.doi.org/10.21474/IJAR01/15410

RESEARCH ARTICLE

EFFICACY AND SAFETY OF RADIOFREQUENCY ABLATION VERSUS ETHANOL ABLATION

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Manuscript Info

Manuscript History
Received: 18 July 2022
Final Accepted: 20 August 2022
Published: September 2022

Key words:-
Radiofrequency, Ablation, Ethanol, Nodule

Abstract

Objectives: Multinodular goiter is the most common thyroid disease in Mongolia. Recent guidelines suggest that a nodule without clinical symptoms should be treated with watchful waiting; however, some patients require treatment because of cosmetic problems or symptoms. The main treatment remainssurgical resection, however, minimally invasive alternatives are being investigated. Ethanol ablation (EA), laser ablation, microwave ablation, and radiofrequency ablation (RFA) are safe and effective techniques for the treatment of nodular goiter. This retrospective review evaluates two widely used methods of ablation in Mongolia, ethanol ablation (EA) methods and RFA. Our objective is to compare volume reduction of single-session EA and RFA for thyroid nodules of different compositions and sizes.

Materials and Methods: This retrospective study was approved by the Research Ethics Committee of the Mongolian National University of Medical Sciences and informed consent was obtained from all patients before EA and RFA. From January 2019 to January 2020, 50 patients with nodular goiter who underwent RFA (mean age 45.74 ±12.45 years) and 50 patients treated with sonography (US)-guided EA (mean age 36.52 ±9.61 years) were enrolled in this study. Nodules were assessed prior to treatment and at 1, 3, 6, and 12 months follow-up. Nodule volume, symptomatic and cosmetic assessmentscores were recorded at each time point. The primaryendpoint was the volume reduction ratio (percentage) at 1, 3, 6, and 12-month follow-ups. Secondary endpoints included therapeutic success rate, improvement of symptoms and cosmetic problems, and a number of major complications.

Results: For the primary outcome of nodule volume reduction, in the RFA and EA groups, the absolute volume reductions at the 12-month follow-up were 62.8±13.2% (50) and 55.8±0.0% (n = 50) respectively. The treatment outcomes are summarized in Tables 3, 4, 5, and 6 and Figures 1, 2, 3, 4, 5, and 6. In RFA group, the mean volume reductions at the 1, 3, 6 and 12-month follow-ups were 33.0±11.0% (n = 50),

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44.7± 17.0% (n = 50), 57.3± 14.7% (n = 50), and 62.8± 13.2% (n = 50), respectively. In EA group, the mean volume reductions at the 1, 3, 6 and 12-month follow-ups were 18.3±0.0% (n = 50), 30.5±0.0% (n = 50), 42.5±0.0% (n = 50), and 55.8±0.0% (n = 50), respectively.

Conclusion: The purpose of this article is to review the current evidence relating to image-guided ablation of thyroid disease with a focus on clinical outcomes and complication rates for patients treated with this minimally invasive approach. EA may be appropriate as the first-line treatment modality for cystic thyroid nodules, which has comparable therapeutic efficacy to, but is less expensive than, RF ablation.

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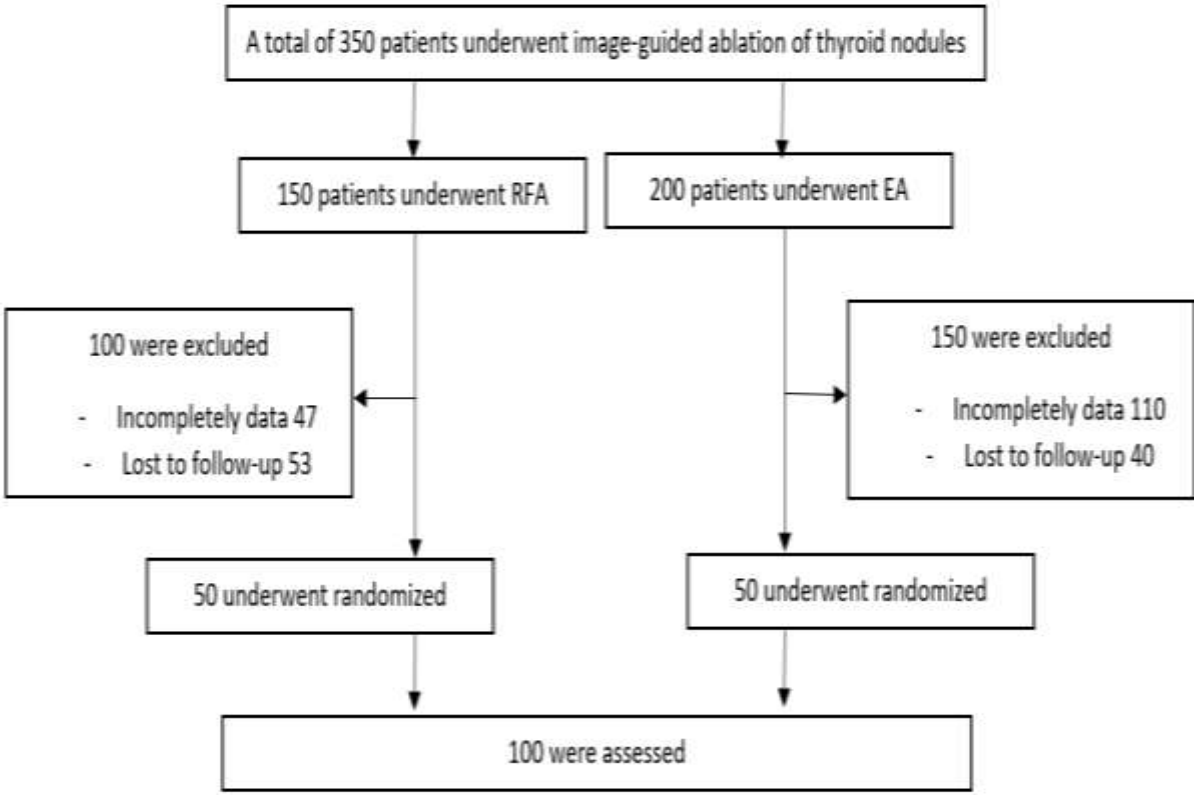
Introduction:-

Multinodular goiter is the most common thyroid disease in Mongolia. A recent epidemiological study has not yet been conducted. Recent guidelines suggest that a nodule without clinical symptoms should be treated with watchful waiting; however, some patients require treatment because of cosmetic problems or symptoms (1, 2). There are several treatment options, but neither is perfect. The main treatment of the disease is still the traditional surgical resection. The most patients with nodules have not been offered alternatives. Ethanol ablation, laser ablation, microwave ablation, and radiofrequency ablation (RFA) are safe and effective techniques for the treatment of nodular goiter (3-5). Ethanol ablation is useful in cystic nodules but not in solid nodules. RFA is useful in different-sized nodules (6). RFA has been widely accepted for the treatment of benign thyroid nodules, goiters, and recurrent thyroid cancers (7-9). But thyroid RFA started in January 2019 in Mongolia. Two approaches have been popularized for the image-guided ablation of thyroid disease, injection of a compound, which is toxic (most commonly ethanol) and is referred to as chemical ablation or energy-based ablation. Image-guided ablation of thyroid disease is increasingly being commonly reported.

Material And Methods:-



Patients

This retrospective study was approved by the Research Ethics Committee of the Mongolian National University of Medical Sciences and informed consent was obtained from all patients before Ethanol and RFA. From January 2019 to January 2020, 50 patients with nodular goiter who underwent RFA (mean age 45.74 ±12.45 years) and 50 patients treated with sonography (US)-guided EA (mean age 36.52 ±9.61 years) were enrolled in this study. Nodules were assessed prior to treatment and at 1, 3, 6, and 12 months follow-up. Nodules volume and symptomatic and cosmetic assessment scores were recorded at each time point. The primary endpoint was the volume reduction ratio (percentage) at 1, 3, 6, and 12-month follow-ups. Secondary endpoints included therapeutic success rate, improvement of symptoms and cosmetic problems, and a number of major complications.

The inclusion criteria were as follows: patients with symptomatic problems due to a thyroid nodule; patients with cosmetic thyroid problems; having refused surgery; cytological confirmation of a benign thyroid nodule on FNAB; no malignant US findings; solid (> 50% solid components) and predominantly cystic (10%< solid components < 50%) thyroid nodules; cystic nodules (< 10% solid components) and serum thyroid hormone and thyrotropin levels within normal ranges.

The exclusion criteria were follicular neoplasm or primary thyroid cancer; history of neck radiation therapy; pregnancy.

Pre-Ablation Assessment

All patients were evaluated by US examination, US-guided biopsy, blood tests, and clinical examinations. US, US-guided biopsy and RF ablation were performed using a 7–15 MHz linear probe and a real-time US system (Mindray M7, China). For each nodule, three orthogonal diameters (the largest diameter and two perpendicular diameters) and the proportion of the solid components were measured.(9) The volume of each nodule was calculated as follows: $V = \pi abc/6$ (where V is the volume, a is the largest diameter, and b and c are the two perpendicular diameters) (10). Laboratory examinations included measurements of serum thyrotropin, total triiodothyronine, free thyroxine, platelet counts, and blood coagulation tests that included prothrombin time and activated partial thromboplastin time. At the time of enrollment, the patients were asked to rate their nodule-related symptoms on a 10-cm visual analog scale (0−10 cm) and a cosmetic grading score was assessed by the physician (1, no palpable mass; 2, no cosmetic problem but a palpable mass; 3, a cosmetic problem on swallowing only; and 4, an easily detected cosmetic problem) (11).

Procedures:-

Ablation Procedures EA and RF ablation were performed with each patient in the supine position and with mild neck extension. No medication was administered before the procedure. All procedures were performed with US guidance. The puncture site was anesthetized with 2% lidocaine, and the skin was not incised. The skin was punctured, and target nodules were approached by using the transisthmic approach method in which the EA needle or the RF ablation electrode is inserted into the short axis of the nodule from the isthmus to the targeting nodule in both EA (12) and RF ablationthis method allows the needle or electrode to pass through a sufficient amount of thyroid parenchyma (13). This technical approach has several advantages. It can prevent a change in the position of the needle or electrode when the patient is swallowing or talking during the ablation and can also prevent fluid leakage (ie, injected ethanol or ablated, hot fluid of the cystic portion of thyroid nodules) to areas outside the thyroid gland. This approach also allows clear, continuous US monitoring of the relationship of the nodule and the needle or electrode tip to the expected location of the recurrent laryngeal nerve, thus minimizing the risks of injury to that nerve and/or the esophagus.

Ethanol ablation:

Ethanol is delivered under ultrasound guidance to lesions that develop an irreversible local injury with infarction, thrombosis, coagulative necrosis, and fibrosis. A 16- or 18-gauge needle was inserted into the nodule through an isthmus. After the needle tip was placed into the central portion of the cyst, the internal fluid contents were aspirated to the maximal extent possible, followed by a slow injection of 99% ethanol into the cystic space. If the cyst contents were viscous, viscous fluid was aspirated by using a large-bore needle (16 gauge) attached to a 50-mL syringe, followed by irrigation with normal saline to remove viscous material attached to the cystic wall, after which ethanol was injected (12, 14). The volume of ethanol injected usually corresponded to 50% of the aspirated volume (12). After 10 minutes of ethanol retention with the needle in place, the injected ethanol was completely removed

and the needle was withdrawn. Following the procedure, each patient was observed for 1 hour while still in the hospital.

RF ablation:
In most patients, one puncture was made in both the skin and the thyroid capsule to prevent leakage of hot fluid from the cyst (20). The RF device used was a cool-tip RF system with a straight-type modified internally cooled electrode: RF generators (Cool-Tip RF system, M-1000, RF Medical, Seoul, Korea) and an 18-gauge internally cooled electrode (RF Medical, Seoul, Korea) with 0.3-, 0.5-, 0.7-, 1-cm active tips, depending on the size of the nodule. Before starting the RF ablation, as much internal fluid as possible was aspirated from the cystic nodule by using the aspiration needle, and then the needle was removed. Ablation was started at 40 W, with a 1-cm active tip, and at 20 W, with a 0.5-cm active tip. If a hyperechoic microbubble did not form at the electrode tip within 5–10 seconds, the RF power was increased in 5- to 10-W increments, up to 70 W. Ablation was terminated when the solid portion of the nodule became hyperechoic and the cystic portion was filled with echogenic bubbles. If a patient complained of pain during the procedure, we reduced the RF power or stopped the ablation (13, 15). Assessment for any possible complications was performed both during and immediately after the procedure to assess its safety (16). After RF ablation, each patient was observed for 24 hours while still in the hospital.

Follow-Ups
Patients were followed up by US and clinical evaluations at 1, 3, 6, and 12 months. The thyroid nodule volume, largest diameter, and cosmetic as well as symptom scores were evaluated in the same manner before and after ablation. The volume reduction ratio was calculated as follows: volume reduction ratio = ([initial volume - final volume] x 100) / initial volume (10). All complications were also evaluated during the follow-up.

Statistical Analysis
The primary outcome was the volume reduction at 1, 3, 6, and 12 months after the RF ablation. Outcomes such as changes in the largest diameter, volume, and symptom score, or the cosmetic score before and after RF ablation were compared by employing the Wilcoxon signed-rank test. Data were analyzed using IBM SPSS, version 21 (IBM Corp., Armonk, NY, USA). Continuous variables are reported as the means± SD with the range. A multiple linear regression analysis was calculated to identify factors that were independently predictive of efficacy (i.e., the volume reductionratioat 1, 3, 6, and 12 months). Variables entered into the model included age, gender, mean energy per mL pretreatment nodule volume, initial nodule volume, and initial nodule solidity. A p-value less than 0.05 was considered statistically significant.

Treatment Outcomes
For the primary outcome of nodule volume reduction in the RFA and EA groups, the absolute volume reduction at the 12-month follow-up was 62.8±13.2% (50) and 55.8±0.0% (n=50) respectively.

The treatment characteristics of our study patients are summarized in Table 2. The mean energy watt was 33.2±9.0 (50). The mean ablation time was 307.0±246.4 (50) seconds.

The treatment outcomes are summarized in Tables 3, 4, 5 and 6, Figures 1, 2, 3, 4, 5, and 6. In the RFA group, the mean volume reductions at the 1, 3, 6 and 12-month follow-ups were 33.0±11.0% (n=50), 44.7±17.0% (n=50), 57.3±14.7% (n=50), and 62.8±13.2% (n=50), respectively.

In the EA group, the mean volume reductions at the 1, 3, 6 and 12-month follow-ups were 18.3±0.0% (n=50), 30.5±0.0% (n=50), 42.5±0.0% (n=50), and 55.8±0.0% (n=50), respectively.

Cosmetic and symptomatic scores
The cosmetic and symptomatic scores are presented in Table 2 and Figures 1, and 2. Before RFA and EA treatment, there were 88% (88/100) patients with nodular-related symptoms, defined as a symptoms score >0. The overall cosmetic score of group RFA and EA improved from 2.6 ± 0.97 (0-3) to 0.9 ± 0.9 (-65.38%) and from 2.2± 0.6 (0-3) to 0.6± 0.97 (-72.72%) at the 12-month follow-up respectively ($p<0.001$) with each group achieving significant improvement ($p<0.001$). The symptomatic score improved in group RFA and EA at the 12-month follow-up evaluation from 3.6 ± 2.2 to 2.1 ± 0.7 (60.1%) and from 4.1 ± 2.5 to 2.1± 0.9 (52.8%) at 12 months $P<0.001$), respectively.

The cosmetic score significantly improved in all subgroups (Figure 5, 6).

The therapeutic success rate in group RFA and EA was 80.0% (40/50) and 69% (34.5/50) at the 12-month follow-up.

Complications and side effects are summarized in Table 7. The overall complication rate was 2.6% (4/150). Major and minor complication rates were 1.3% (2/150) and 1.3% (2/150), respectively. All study subjects recovered without sequelae. Therefore, no patient experienced a life-threatening or delayed complication during the follow-up.

Discussion:-

The results of our study showed that RFA induced a significant reduction in nodule volume and relief of symptomatic and cosmetic problems.

In this study, mean volume reduction was significant after a single session of RFA, but it was not significant in the EA group. In the EA group, mean nodule volume had decreased slightly by the 12-month follow-up evaluation, but the difference was not statistically significant.

Deandrea et al. [10] reported a 46.3% volume reduction at the 6-month follow-up evaluation after RFA.

This finding agrees with the results of our previous retrospective study [11], in which we found that 1 and 3 months after RFA, the volume of predominantly solid nodules had decreased slowly compared with that of predominantly cystic thyroid nodules. The 6-month follow-up data, however, showed that the volume reduction did not differ significantly in the solid and the cystic nodules.

In this study, the symptoms and cosmetic concerns were resolved in all patients after RFA. The clinical problems in the control group, however, had no statistically significant resolution Papini et al. [34] reported local symptom aggravation in 45% of untreated patients at the 12-month follow-up evaluation. Dosing et al. [33] reported no relief of symptoms or cosmetic problems in the control group. Therefore, in patients with large, symptomatic, predominantly solid thyroid nodules, the likelihood that the nodule will progress and that the symptoms will worsen is high if the observation is chosen.

The principal limitation of our study was the relatively short follow-up period. A long-term follow-up study is recommended for evaluating the efficacy and detecting unexpected complications of RFA.

The results confirm that RFA is effective in reducing nodule volume and relieving nodule-related clinical problems and that on the basis of findings in a comparable control group, an effect due to spontaneous nodule reduction can be excluded.

Conclusion:-

The purpose of this article is to review the current evidence relating to image-guided ablation of thyroid disease with a focus on clinical outcomes and complication rates for patients treated with this minimally invasive approach.

EA may be the first-line treatment modality for cystic thyroid nodules, which has comparable therapeutic efficacy to but is less expensive than, RF ablation.

Ethical statement

The study was approved by the Research Ethics Committee of the Mongolian National University of Medical Sciences) (No 2019/9-05). All patients provided written informed consent before participating in the study

Table 1:- Demographic Characteristics of Enrolled Patients.

Characteristic	Radiofrequency Ablation Group	Ethanol Ablation Group	p
Sex (M/F)	5/45 (10%/90%)	2/48 (4.2%/95.8%)	1.00
Age (y)	45.74±12.45 (17-65)	36.52±9.61 (17-64)	0.06
Follow-up period (mo)	12	12	0.31

Triiodothyronine (ng/dL)	113.18±18.51 (72–149)	104.59±13.81 (79–124)	0.11
Free thyroxine (ng/dL)	1.49±0.31 (0.90–1.90)	1.52±0.22 (0.90–1.80)	0.84
Thyrotropin (μIU/L)	1.50±0.82 (0.81–3.67)	1.50±0.61 (0.47–2.35)	0.41
Needle size	0.696	-	
Mean nodule diameter (cm)	1.79±1.5 (0.17-3.21)	1.45±0.4 (0.8-2.4)	
Mean nodule volume (ml)	4.86 (10.0)	1.94 (12.3)	
Mean largest nodule diameter (cm)	3.38 (3.01)	2.4 (1.7)	
Symptom score	3.6±2.2 (0-10)	4.1±2.5 (0-10)	0.60
Cosmetic grade	2.6±0.97 (0-3)	2.2±0.6 (0-3)	0.68
Number of patients with number of treated nodules	50 with 50	50 with 50	

Table 2:- Treatment Characteristics of 50 Thyroid Nodules Analyzed.

	RFA ablation
RF power (W)	33.2±9.0 (50)
Ablation time (second)	307.0±246.4 (50)
Total energy	1660.8 (50)
Energy/mL (J)	3.6±0.0 (50)
Number of RF sessions	50
Solid component	
Solid	14
Predominantly solid	10
Sponge	14
Cyst	5
Predominantly cystic	7

Table 3:- Outcome of group RFA composition difference.

	Baseline composition of nodules					
	solid	**predominantly solid**	**sponge**	**cyst**	**predominantly cyst**	**Total**
Nodule volume (ml)						
Baseline	4.5±2.0 (14)	5.6±1.9 (10)	4.5±1.6 (14)	3.0±1.0 (5)	6.4±4.1 (7)	
1 Month	2.5±1.6 (14)	4.9±1.4 (10)	3.1±1.7 (14)	2.2±1.3 (5)	3.5±2.6 (7)	
3 Months	2.3±1.2 (14)	5.1±1.4 (10)	2.1±1.7 (14)	0.8±0.4 (5)	2.5±2.1 (7)	
6 Months	2.1±0.9 (14)	4.3±1.4 (10)	1.3±1.1 (14)	0.5±0.3 (5)	1.6±1.2 (7)	
12 Months	2.1±0.8 (14)	3.9±1.2 (10)	0.9±0.6 (14)	0.2±0.1 (5)	1.2±0.5 (7)	
Nodule volume (%)						
1 Month	44.2±0.0 (14)	13.1±0.0 (10)	32.6±0.0 (14)	26.3±0.0 (5)	45.5±0.0 (7)	**33.0±11.0**
3 Months	48.8±0.0 (14)	9.3±0.0 (10)	53.5±0.0 (14)	73.7±0.0 (5)	61.0±0.0 (7)	**44.7±17.0**
6 Months	53.5±0.0 (14)	24.3±0.0 (10)	70.9±0.0 (14)	84.2±0.0 (5)	74.8±0.0 (7)	**57.3±14.0**
12 Months	53.8±0.0 (14)	30.8±0.0 (10)	79.1±0.0 (14)	91.2±0.0 (5)	82.1±0.0 (7)	**62.8±13.2**

Table 4:- Outcome of group RFA size difference.

	Baseline size of treated nodules			
	small	**medium**	**large**	**very large**
Nodule volume (ml)	**(≤5 ml)**	**(>5 to ≤10 ml)**	**(>10 to ≤15 ml)**	**(>15 ml)**
Baseline	1.4±2.9 (30)	7.2±2.4 (12)	11.4±1.6 (4)	17.7±3.1 (4)

1 Month	0.9±1.9 (30)	4.0±2.8 (12)	9.5±6.97 (4)	12.6±9.9 (4)
3 Months	0.8±1.4 (30)	2.8±3.7 (12)	8.4±11.9 (4)	11.0±12.1 (4)
6 Months	0.6±1.4 (30)	1.8±3.1 (12)	7.6±14.9 (4)	8.3±7.9 (4)
12 Months	0.5±1.6 (30)	1.4±2.5 (12)	7.1±16.3 (4)	6.9±8.8 (4)
Nodule volume (%)				
1 Month	-35.71±0.0 (30)	-44.4±0.0 (12)	-16.7±0.0 (4)	-28.8±0.0 (4)
3 Months	-42.86±0.0 (30)	-61.1±0.0 (12)	-26.3±0.0 (4)	-37.9±0.0 (4)
6 Months	-57.1±0.0 (30)	-75.0±0.0 (12)	-33.3±0.0 (4)	-53.1±0.0 (4)
12 Months	-64.29±0.0 (30)	-80.6± 0.0 (12)	-37.7±0.0 (4)	-61.0±0.0 (4)

Table 5:- The outcome of group EA composition difference.

	Baseline composition of nodules					
	solid	**predominantly solid**	**sponge**	**cyst**	**predominantly cyst**	
Nodule volume (ml)						
Baseline	2.9±1.6 (10)	1.5±0.8 (10)	2.8±1.5 (10)	1.8±0.5 (10)	0.7±0.1 (10)	
1 Month	2.7±0.8 (10)	1.4±0.2 (10)	2.6±0.4 (10)	0.7±0.3 (10)	0.7±0.0 (10)	
3 Months	2.5±0.2 (10)	1.3±0.1 (10)	2.4±0.2 (10)	0.3±0.1 (10)	0.6±0.0 (10)	
6 Months	2.4±0.2 (10)	1.1±0.1 (10)	1.7±0.2 (10)	0.2±0.1 (10)	0.4±0.0 (10)	
12 Months	2.1±0.1 (10)	1.0±0.1 (10)	1.3±0.1 (10)	0.2±0.1 (10)	0.2±0.0 (10)	
Nodule volume (%)						
1 Month	5.6±0.0 (10)	8.7±0.0 (10)	5.4±0.0 (10)	63.4±0.0 (10)	8.2±0.0 (10)	**18.3±0.0**
3 Months	13.2±0.0 (10)	15.3±0.0 (10)	13.4±0.0 (10)	85.8±0.0 (10)	24.7±0.0 (10)	**30.5±0.0**
6 Months	17.0±0.0 (10)	24.0±0.0 (10)	40.1±0.0 (10)	87.4±0.0 (10)	43.8±0.0 (10)	**42.5±0.0**
12 Months	27.4±0.0 (10)	36.0±0.0 (10)	54.5±0.0 (10)	88.5±0.0 (10)	72.6±0.0 (10)	**55.8±0.0**

Table 6:- The outcome of group EA size difference.

	Baseline size of treated nodules			
	small	**medium**	**large**	**very large**
Nodule volume (ml)	**(≤5 ml)**	**(>5 to ≤10 ml)**	**(>10 to ≤15 ml)**	**(>15 ml)**
Baseline	1.6±0.8 (46)	5.7±0.8 (4)	-	-
1 Month	1.3±0.4 (46)	5.3±0.4 (4)	-	-
3 Months	1.1±0.1 (46)	4.7±0.1 (4)	-	-
6 Months	1.0±0.1 (46)	3.0±0.1 (4)	-	-
12 Months	0.8±0.1 (46)	2.3±0.1 (4)	-	-
Nodule volume (%)				
1 Month	-20.4±0.0 (46)	-7.7±0.0 (4)	-	-
3 Months	-31.5±0.0 (46)	-17.2±0.0 (4)	-	-
6 Months	-37.7±0.0 (46)	-47.3±0.0 (4)	-	-
12 Months	-48.8±0.0 (46)	-60.5±0.0 (4)	-	-

Figure 1:- RFA, Subgroup analysis of nodule volume reduction ratio at 1, 3, 6, and 12 months according to different baseline nodule characteristics based on initial size.

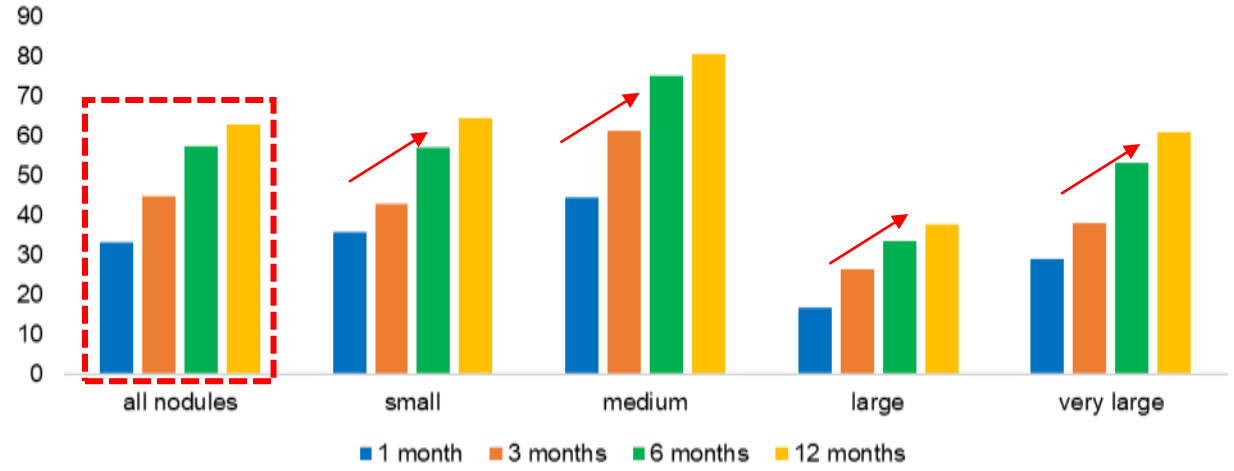


Figure 2:- RFA, Subgroup analysis of nodule volume reduction ratio at 1, 3, 6, and 12 months according to different baseline nodule characteristics based on initial nodule composition.

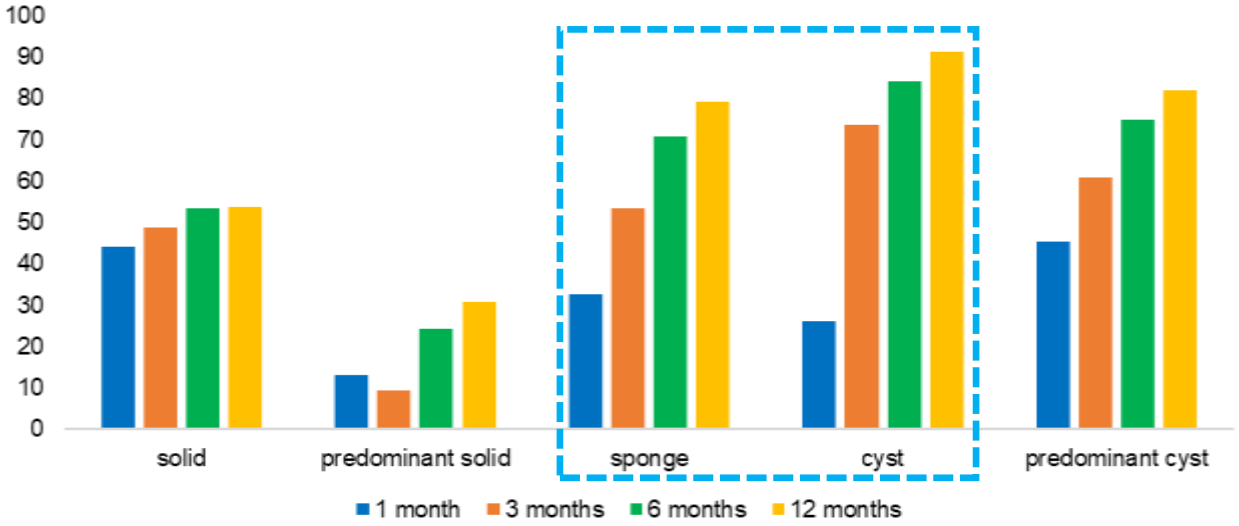


Figure 3:- EA, Subgroup analysis of nodule volume reduction ratio at 1, 3, 6, and 12 months according to different baseline nodule characteristics based on initial size.

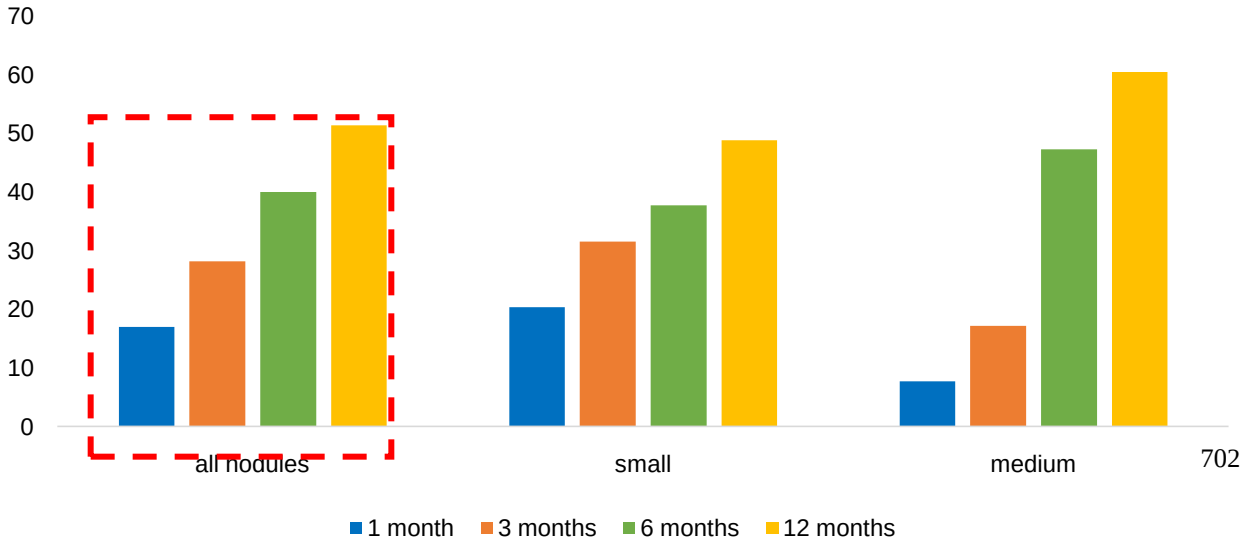


Figure 4:- EA, Subgroup analysis of nodule volume reduction ratio at 1, 3, 6, and 12 months according to different baseline nodule characteristics based on initial nodule composition.

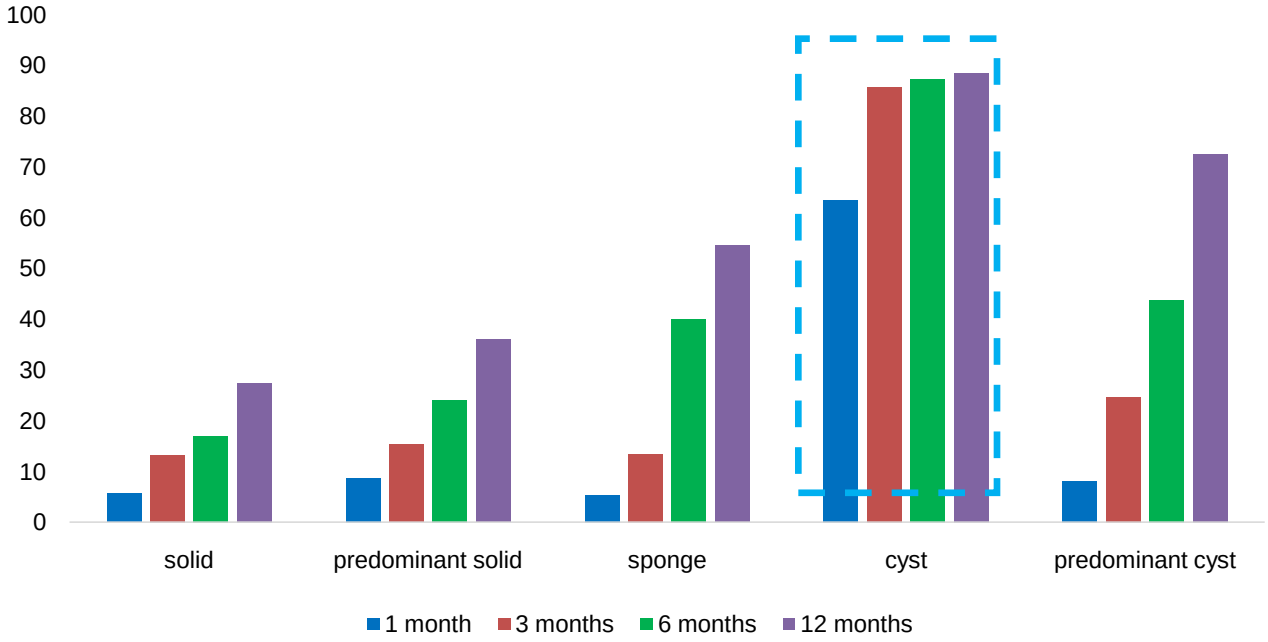


Figure 5:- RFA group, Percentage of patients and their outcomes in terms of volume reduction ratio, cosmetic and symptom scores at baseline, 1, 3, 6, and 12 months.

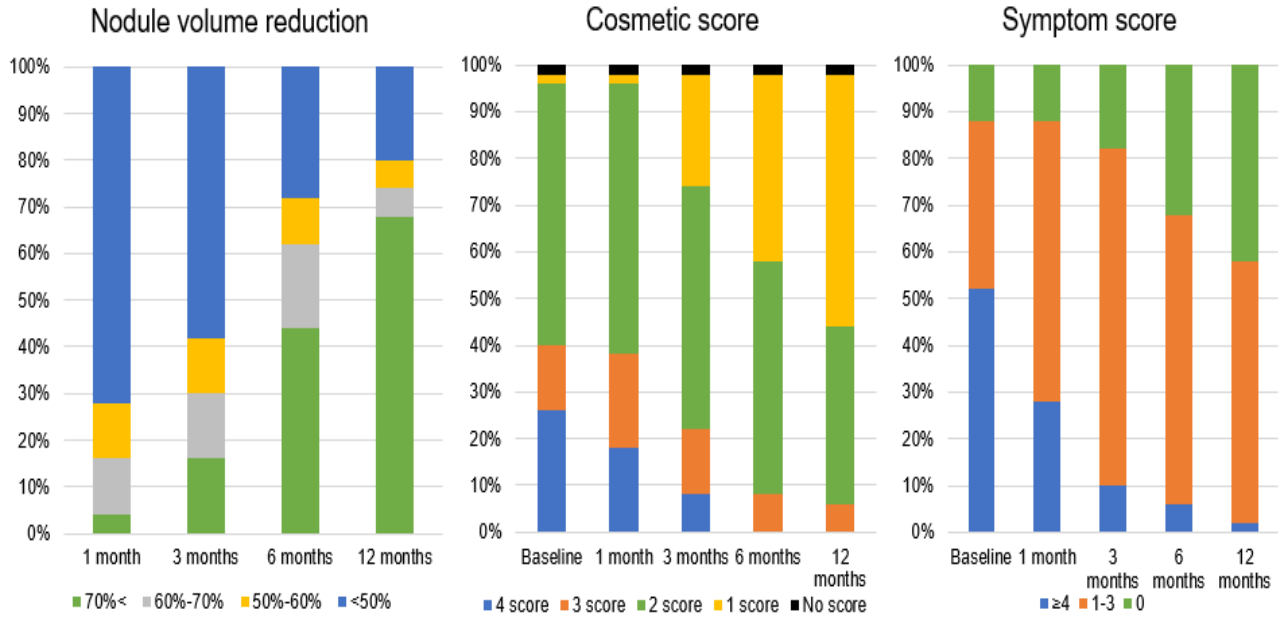


Figure 6:- EA group, Percentage of patients and their outcomes in terms of volume reduction ratio, cosmetic and symptom scores at baseline, 1, 3, 6 and 12 months.

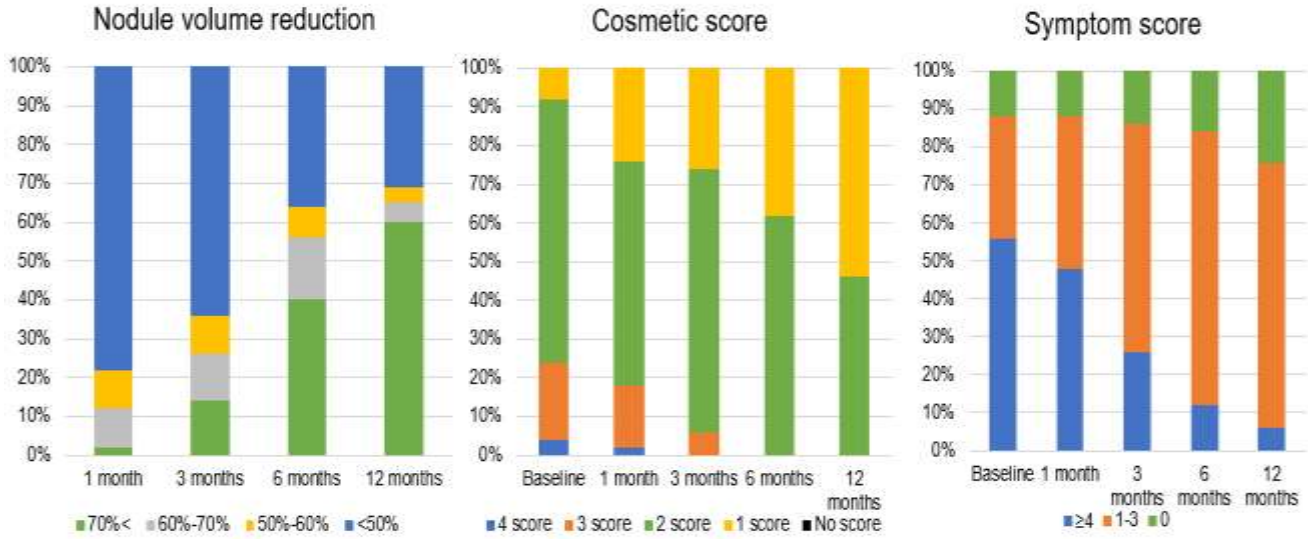


Table 7:- Complications

Complications	Number of Complications (%)	Time of Detection (Days)	Time to Recovery (Days)
Major complications (n = 3)			
Transient voice change	2 (1.3)	1	60
Hypothyroidism	1 (0.7)	30	30
Minor complications (n = 1)			
Hematoma	1 (0.7)	1	7
Total	4 (2.6)	1–30	1–60

Table 8:- Multiple Linear Regression Analysis of Factors Independently Predictive of Volume Reduction.

Regression Statistics	
Multiple R	0.996
R Square	0.992
Adjusted R Square	0.966
Standard Error	0.756
Observations	50

ANOVA

	df	*SS*	*MS*	*F*	*Significance F*
Regression	10	2927.7	292.8	512.5	0.0
Residual	40	22.8	0.6		
Total	50	2950.5			

	Coefficients	*Standard Error*	*t Stat*	*P-value*	*Lower 95%*	*Upper 95.0%*
Intercept	0	#N/A	#N/A	#N/A	#N/A	#N/A
Age	0.01	0.01	0.56	0.58	-0.01	0.02
Gender	-0.25	0.35	-0.73	0.47	-0.95	0.45
Composition of nodule	-0.06	0.08	-0.68	0.50	-0.22	0.11
Ablation time,	0.05	0.04	1.20	0.24	-0.03	0.13
Ablation W	-0.01	0.02	-0.49	0.63	-0.06	0.04
Needle size	0.94	0.64	1.46	0.15	-0.36	2.24
Before RFA	-0.05	0.03	-1.69	0.10	-0.11	0.01
1 month after	0.31	0.06	5.46	0.00	0.20	0.43
3 months after	-1.10	0.08	-13.87	0.00	-1.26	-0.94
6 months after	1.89	0.06	32.01	0.00	1.77	2.01

Table 9:- Correlation matrix.

	12 months after	Age	Gender	Composition of nodule	Ablation time,	Ablation W	Needle size	Before RFA	1 month after	3 months after	6 months after
12 months after	1										
Age	0.0	1.0									
Gender	-0.3	0.2	1.0								
Composition of nodule	0.0	-0.1	0.1	1.0							
Ablation time,	0.5	-0.1	-0.1	0.0	1.0						
Ablation W	0.2	0.1	0.0	0.1	0.3	1.0					
Needle size	0.1	-0.2	-0.1	0.0	0.2	0.1	1.0				
Before RFA	0.6	0.0	-0.1	0.1	0.7	0.3	0.1	1.0			
1 month after	0.7	0.0	-0.2	0.1	0.7	0.2	0.2	0.9	1.0		
3 months after	0.8	0.1	-0.3	0.0	0.6	0.2	0.2	0.8	0.9	1.0	
6 months after	1.0	0.0	-0.3	0.0	0.5	0.2	0.2	0.7	0.8	1.0	1.0

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