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The Role of Radiofrequency Ablation as an Alternative Tool in Management of Symptomatic Benign Thyroid Nodules

Esraa Mahmoud Ahmad
Internal Medicine Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt

Hanan Mohamed Amer
Internal Medicine Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt

Rania Sayed Abd EL Baky
Internal Medicine Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt

Mehran Samy Nasr
Internal Medicine Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt

Ahmed Mohamed Hussein
Interventional Radiology Department, Radiology Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt

Salah Hussein EL Halawani
Internal Medicine Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt

***Abstract*---**Aim of the work: To assess the role of radiofrequency ablation as an alternative tool in management of symptomatic benign thyroid nodules. Methods: We assessed non-functioning benign thyroid nodules in 10 patients, after treatment by radiofrequency (RF) ablation and follow-up for 6 months. RF ablation was done by Cool-Tip RF system and cooled internal electrode. Nodule volume, cosmetic and symptom scores were calculated earlier prior to treatment and throughout the follow-up. We assessed all efficacy related factors and reported complications. Results: A statistically significant difference existed between volume of nodules before the procedure with mean volume was 22.20 ± 4.61 and 1 month after with mean volume 12.38

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***Corresponding author**: Ahmad, E. M.; Email: dr_esraa_gamal@yahoo.com*
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± 2.91with mean reduction ratio of 44.27 ± 5.77% and 3 months after the procedure with mean volume 8.08 ± 2.92 with mean reduction ratio of 65.14 ± 8.92%, also 6 months after procedure with mean volume 6.90 ± 2.78 with mean reduction ratio of 71.10 ± 7.71 %. The symptoms were significantly improved after RF ablation of patients complaining of compressive and cosmetic problems.

***Keywords*---**benign, cosmetic dissatisfaction, non-surgical management, pressure effects, radiofrequency ablation, thyroid nodule.

Introduction

Thyroid nodules (TNs) are detected frequently and are commonly known to be present in 20–76% of the general population. Thyroid nodules are nodules which commonly arise within an otherwise normal gland. They may be hyperplastic or tumorous, but only a small percentage of thyroid tumors (5%–15%) are malignant. Small, asymptomatic nodules are common, and often go unnoticed. Nodules that grow larger or produce symptoms may eventually need medical care. Thyroid surgery almost always requires hospitalization and anesthesia. Therefore, minimally invasive alternatives have been explored. Ethanol ablation, laser ablation, microwave ablation, and radiofrequency ablation (RFA) are safe and effective techniques for the treatment of nodular goiter. Radiofrequency (RF) ablation has been gaining popularity as a minimally invasive treatment for benign thyroid nodules. RF ablation can be used to treat both benign thyroid nodules and inoperable, recurrent thyroid cancers located in the surgical bed as well as lymph nodes.

Aim of the work

To assess the role of radiofrequency ablation as an alternative tool in management of symptomatic benign thyroid nodules.

Patient and methods

The institutional review board of Ain Shams University Hospitals approved this study, our patients received written informed consent prior to the US-guided Fine Needle Aspiration Biopsy (FNAB) and RF ablation.

Patients

Between August 2019 and September 2021, 10 patients were ablated under US-guidance at Ain Shams University Hospitals. patients were included when they meet the following conditions: Cosmetic or compressive problems, such difficulty in swallowing or breathing; largest nodule diameter of more than 16 ml, ultrasound guided biopsies confirming that the nodule is benign; absence of suspicious US characteristics; normal ranges of full thyroid laboratory profile; refusal of or unfit for surgery. This ended by choosing 10 patients (3 men, 7 women; age ranging between 22-82 years).

Exclusion criteria

Allergy to local an aesthetics, FNA non-contributory or suspicious nodule, taking a treatment with anticoagulant (INR: more than 1.5, platelet: less than 50000) and pregnant and breastfeeding women.

Pre-ablation evaluation

Thyroid nodules were assessed by US examination, laboratory and FNAB. Diagnostic US, US- guided biopsy and RF ablation were conducted using a 10-MHz linear probe (Aplio 400, Toshiba Medical System and Logic P9, GE medical systems). FNAB was performed four days before the RF session. Preceding the FNAB, proper history taking for certain drugs such as Aspirin or Plavix was carried out. Three measurements of each nodule in three orthogonal planes were measured prior to the procedure. The nodule volume was measured as V = n abc/6 (where V is volume, a is the largest plane, while b and c are the two other planes). Vascularity of the nodule was classified using a scale of four points, with Doppler findings as follows: No Doppler signal, signals in less than 25% of the nodule, or 25-50% of the nodule and in more than 50% of the nodule. Laboratory tests included measurements of serum thyrotropin, total triiodothyronine, free thyroxine as well as platelet count, pro- thrombin time and activated partial thromboplastin time. Patients were asked to rate through a visual analogue scale from pressure symptoms and cosmetic complain on a (0-10).

Procedure

The patient is placed in the supine position with the neck extended. Local anesthesia is administered at the site of ablation and thyroid capsule, Hydro dissection is performed with local anesthesia mixed with HCO3 then 5% dextrose, either under the skin (to prevent skin burns) or to distance other critical structures near the ablation zone. The specialized RFA electrode is inserted under Ultrasound guidance, RFA of the nodule starts and is monitored by ultrasound in real time, The skin was not incised so as to prevent unnecessary scar formation. An electrode was inserted into the thyroid nodule under US guidance along the short axis of the nodule. Initially, the electrode tip was positioned in the deepest and most remote portion of the nodule. Ablation began with 25-30 W of power. However, the power was reduced to 20–25 W if the patient could not tolerate the pain during ablation.

If the formation of a transient hyperechoic zone at the electrode tip did not appear within 10 s, power was increased in 5-10-W increments up to 70 W. When a transient hyperechoic zone appeared at the periphery of the nodule (usually within 5–10 s), the electrode tip was moved backward in order to prevent heat transmitting to the perithyroidal tissue. In the more central areas of the nodule, if the transient hyperechoic zone expanded around the electrode tip, the electrode was moved to an untreated area. Before ablation, we divided the nodule into multiple imaginary or supposed ablating units. The nodule was then treated unit by unit using the moving shot technique. During ablation, both thighs were checked frequently to prevent skin burn.

The ablation shouldn't exceed 20 mins to prevent patient discomfort. Ablation was terminated when all units of the nodule had changed to transient hyperechoic zones, do not ablate more than necessary to avoid damage to adjacent structures, after ablation, oral analgesics (acetaminophen) were prescribed. If the patient complained of pain into the next day, additional oral analgesics were prescribed.

Statistical Evaluations: Recorded data were analyzed using the statistical package for social sciences, version 20.0 (SPSS Inc., Chicago, Illinois, USA). Quantitative data were expressed as mean± standard deviation (SD). Qualitative data were expressed as frequency and percentage. The following tests were done: Paired sample t-test of significance was used when comparing between related sample, a one-way analysis of variance (ANOVA) when comparing between more than two means, post Hoc test: Least Significant Difference (LSD) was used for multiple comparisons between different variables, the confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value was considered significant as the following: Probability (P-value), P-value <0.05 was considered significant, P-value <0.001 was considered as highly significant, P-value >0.05 was considered insignificant.

Results

The research involved a total of ten patients with the age ranging from 22-82 years old, the mean was 50.70 years old (SD ± 17.09). Among them 7 patients (70%) were females and 3 patients (30%) were males. There was statistically significant difference between volume of nodules before the procedure with mean volume was 22.20 ± 4.61 and 1 month after with mean volume 12.38 ± 2.91with mean reduction ratio of 44.27 ± 5.77% and 3 months after the procedure with mean volume 8.08 ± 2.92 with mean reduction ratio of 65.14 ± 8.92%, also 6 months after procedure with mean volume 6.90 ± 2.78 with mean reduction ratio of 71.10 ± 7.71 %. Patients with compressive and aesthetic problems saw a considerable reduction in their symptoms after RF ablation, The median score for compressive symptoms was dramatically lower; it was 4 after one month, 2 after three months, and 0 after six months compared to 8 before the RF ablation P value <0.001. The median score for cosmetic issues compared to 4 before therapy, there were 2 at 1 month, 1 at 3 months, and 1 at 6 months P value <0. 001.US structure with spongiform nodules showing mean reduction ratio 76.80 % at 6 months vs 63.00 % and 69.00 % for mixed &solid nodules respectively. At the beginning of the study, all of the patients were euthyroid and had normal thyroid function tests after 1, 3, and 6 months. During the study, seven out of ten participants did not have any complications. One of the ten patients experienced a serious problem shortly after the operation, which was voice changes. The alterations in voice were just temporary, and they returned to normal after around 3 hours. Minor problems occurred in two of the individuals. During the ablation, one of them got a first-degree burn. With topical therapy, it healed fully without scarring after approximately a month. The other patient got a tiny hematoma, which disappeared the next day after around 3 hours. There were no life-threating complications.

Table (1) shows that the median score for compressive symptoms was dramatically lower; it was 4 after one month, 2 after three months, and 0 after six months compared to 8 before the RF ablation P value <0.001. The median score for cosmetic issues compared to 4 before therapy, there were 2 at 1 month, 1 at 3 months, and 1 at 6 months P value <0. 001.

Table (2) shows that there was statistically significant decline seen in volume in the study group score at 1 month than pre procedure with mean difference of -9.82 ± 2.36 and p-value < 0.001, and also decreased at 3 months than pre procedure with mean difference of -14.12 ± 2.82 and p-value < 0.001. Finally, the volume score was decreased at 6 months by -15.30 ± 2.72 than pre procedure with p-value < 0.001. Table (3) shows that the volume reduction ratio (%) was statistically significant P value < 0.001. The mean VRR± SD was 44.27 ± 5.77 at 1 month of procedure, 65.14 ± 8.92 at 3 months, and 71.10 ± 7.71 at 6 months.

Table (4) shows that there was statistically significant relation found between Echo-structure and volume pre, one month, three months, and six months with p-value 0.182, 0.068, 0.025 and 0.099 respectively. There was statistically significant difference found between Echo-structure distribution and volume reduction ratio at 1 month, 3 months and 6 months with p-value 0.025, 0.009 and 0.017. It is clear from the table that there is noticeable improvement in E2. Table (5) During the follow-up period, no changes in hormonal parameters were observed. At the beginning of the study, all of the patients were euthyroid and had normal thyroid function tests after 1, 3, and 6 months. Table (6): shows the complications happened in the 10 patients.

Figure 1: illustrates the extent of the difference in volume (ml) in the study group over time.
Figure 2:demonstrates the relationship of echo structure with volume and reduction ratio among the studied patients.
Figure 3: shows the hormonal parameters (FT3, FT4, TSH) follow up after 1, 3 and 6 months.
Figure 4: Shows the complications happened in the 10 patients.

Discussion

Thyroid nodules are frequent among the general population. Ultrasound is the most commonly used imaging technique in the evaluation of thyroid nodules and its use has increased the discovery of nodules greatly. Large thyroid nodules may become responsible for pressure symptoms, resulting in neck discomfort, cosmetic complaints, and decreased quality of life. Partial/total thyroid surgery has so far constituted the only therapeutic approach for these. Although surgery is widely available, highly effective, and safe in skilled centers, complications (both temporary and permanent) still occur in 2–10 % of cases Hypothyroidism is an unavoidable effect after total thyroidectomy, requiring lifelong levo-thyroxine replacement therapy. Besides, surgery may not be recommended for high-risk patients or refused by others.

Radiofrequency ablation (RFA) is a relatively new technique that seems a safe and effective method for the debulking of large benign thyroid nodules and a

promising treatment modality for autonomously functioning nodules. The aim of this study is to evaluate the efficacy and safety of RF ablation in benign thyroid nodules with correlation between volume reduction of the nodules and some common US features. Radiofrequency ablation cannot remove thyroid nodules immediately; rather, it induces the necrosis and gradual involution of thyroid nodules, resulting in volume reduction and improvements in clinical symptoms, with the efficacy of RF ablation being similar to that of thyroid surgery.

RF ablation resulted in a considerable improvement in the symptoms of patients complaining of compressive and aesthetic issues related to the presence of pathologically verified benign thyroid nodules after receiving RF ablation of these nodules; the median score for compressive symptoms was dramatically lower; it was 4 after one month, 2 after three months, and 0 after six months compared to 8 before the RF ablation P value <0.001. The median score for cosmetic issues compared to 4 before therapy, there were 2 at 1 month, 1 at 3 months, and 1 at 6 months P value <0. 001.

MOHAMMED & AHMED (2020), conducted a study on 20 patients with non-functioning benign thyroid solid nodules between March 2016 and April 2018, after treatment by radiofrequency (RF) ablation and follow-up for 12 months. Nodule volume, cosmetic and compressive symptoms scores were calculated earlier prior to treatment and throughout the follow-up. Of the 20 patients, 2 men and 18 women, age ranging from 19 to 69, all suffered from compressive symptoms or cosmetic complains prior to RFA. The median score for compressive symptoms was dramatically lower; it was 1 compared to 6 before RF ablation, P value <0.001. The median of the cosmetic problem scoring was 2 compared to 5 before treatment P value <0.001. Another study done by Deandrea et al. (2019), studied 337 patients with solid cold benign thyroid nodules from six Italian institutions From January 2014 to December 2016. At follow-up appointments, all patients were asked to score their pressure symptoms on a 10 cm visual analogue scale (grade 0–10 cm). The median score for compressive symptoms was dramatically lower; it was 0.61 compared to 6.2 before RF ablation, P value <0.001. The median of the cosmetic problem scoring was 1.66 compared to 3.15 before treatment P value <0.001. This study showed that RF ablation resulted in a significant reduction in the volume of the benign thyroid nodules. The mean VRR± SD was 44.27 ± 5.77 at 1 month of procedure, 65.14 ± 8.92 at 3 months, and 71.10 ± 7.71 at 6 months. Deandrea et al. (2019), found a correlation between nodule basal volume and shrinkage. The maximum benefit of volume reduction ratio was reported to be 69 to 90% and was showed at 6 to 9 months. He found that the median basal volume was 20.7 mL, and this significantly decreased after RFA at 6 months (7.3 mL (−63.5%) and at 12 months (6 mL (−70%), P vs 6 months = 0.009). Another study done by Ahn et al. (2021), which included A total of 22 benign thyroid nodules from 19 patients treated with RF ablation between March 2010 and January 2013. The internal and external factors of these nodules were retrospectively reviewed and correlated with the therapeutic success and the volume reduction ratio (VRR). The volume and size of the nodules were determined before treatment, and the VRR was calculated at 6-month and 1-year follow-up examinations after RF ablation. The size and volume of the thyroid nodules significantly decreased from the initial US findings, the size decreased from 3.9±1.1 cm before ablation to 2.6±0.9 cm and 2.3±0.8 cm at the 6-month

and 1-year follow-up, respectively. The mean VRRs were 66.1±18.7% at 6 months and 74.3±16.7% at 1 year. The therapeutic success rate after 6 months and 1 year was 81.8% and 90.9%, respectively. The composition of thyroid nodules by US and the VRR were shown to have a strong relationship in our study. The microcystic nodules (E2) showed the best VRR compared to cystic nodules (E1) and completely solid nodules (E3). The microcystic nodules (E2) achieving the greatest mean volume reduction 76.80 % in comparison to 69.00 % and 63.00 % in completely solid (E3) and cystic nodules (E1) respectively. Our results were similar to the results reported by Kim et al. (2015), who studied 201 thyroid nodules with sponge-like appearance from 195 patient. He reported that microcystic nodules (also called spongiform) and the grossly cystic ones shrank better (>75% of the total nodule volume) than the nodules with a homogeneous solid US pattern. This was not in line with results reported by Jeong et al. (2008), which included A total of 302 benign thyroid nodules in 236 euthyroid patients were treated with US-guided RFA between June 2002 and January 2005. The composition of the nodules was assessed subjectively by an US examiner, and was classified as mainly solid, mainly cystic and mixed type. The nodules that had a solid portion greater than 80% were defined as mainly solid type (n=164), those that had a cystic portion greater than 80 % were defined as mainly cystic type (n=49), and the others were defined as a mixed type if they were neither mainly solid nor cystic (n=89). He reported that at 1 and 3 months' follow-up, cystic nodules decreased in size more than the other types (solid, mixed type), (P = 0.000, 0.007 and 0.009 respectively), but there was no significant difference between the types of the nodules regarding VRR (either cystic, solid or mixed nodules) at 6 months' follow-up (P = 0.621). And this agreed with the results reported by Kim et al. (2015), who studied 201 thyroid nodules and found that the presence of coarse calcifications did not influence the RFA outcome at 6 or 12 months (P 0.68 and 0.94 respectively); no difference was found in nodule's reduction after RFA. Our results also were in agreement with results reported by Ahn et al. (2021), which included A total of 22 benign thyroid nodules from 19 patients treated with RF ablation between March 2010 and January 2013 which found that calcifications were not significantly correlated with VRR (P>0.05).

We found no correlation between the vascularity of thyroid nodules measured by ultrasound and the VRR in our study (P = > 0.05). This finding was in agreement with results reported by El-Galil et al. (2021), which included A total of 45 benign thyroid nodules of 40 patients treated with radiofrequency ablation and followed up for 6 months. Which found that during the follow-up, there was no significant relation between the vascularity of the thyroid nodules by US and the VRR. On the other hand, Deandrea et al. (2019), found a correlation between basal volume and US pattern of the nodules and final shrinkage. He reported that regarding vascularization, The intra- and perinodular patterns (v2) resulted in a more favourable outcome than both intense (v1) and weak perinodular patterns (v3) at 6 months (62% reduction vs 56% and 50% respectively, $P < 0.01$) and at 1-year follow-up (71% vs 68.8% and 67.9% respectively, $P < 0.03$). The possible explanation of this observation is that heating produces more steam in the case of tissue with a large fluid component, colloid or blood and that the steam enhances the thermocoagulative process in the treated nodule. This mechanism may be shared by all thermoablative techniques, whatever the heating source: LA (laser

ablation), RFA (Radiofrequency ablation), HIFU (high intensity focused ultrasound), microwaves and so on.

In our study we did not show a significant change of Serum levels of TSH, FT3 and FT4 6 months after RFA. And this agreed with the results reported by Rabuffi et al. (2019), which included A total of 77 patients with solid cold benign thyroid nodules treated with RFA in a single center between 2013 and 2016. Nodule volume, thyroid nodule related compressive symptoms, cosmetic concerns and thyroid function were evaluated. Which found that during the follow-up, there was no immediate or late changes in thyroid function were observed. Twelve months following therapy, all of the patients were euthyroid.

During the RFA procedure, one patient developed a major complication it was a transient voice changes which was fully recovered immediately after the procedure. Also, Minor problems occurred in two of the individuals. During the ablation, one of them had a first-degree burn, which healed totally without scarring. The other patient got a minor hematoma, which went away on its own at the same day. Hamidi et al. (2018), reported that RF ablation could be an alternative to surgery in the management of both toxic and non-toxic benign thyroid nodules as the procedure had no sustained complications through a study done on 14 patients with benign thyroid nodules predominantly solid TNs treated with RFA at Mayo Clinic in Rochester, Minnesota, from December 1, 2013, till October 30, 2016. Deandrea et al. (2019), studied 337 patients with solid cold benign thyroid nodules. A total of 238 patients (71.6%) experienced no complications at all, 45 (13%) complained of minimal side effects as pain and cough, 52 (15%) had minor complications as Oedema and Superficial hematoma, 2 (0.4%) experienced major complications as Voice change and Nodule infection. All patients had a complete recovery without any permanent side effects.

Conclusion

Our work, suggests that RFA is an efficient option to surgery in reducing the size of compressive benign thyroid nodules and their associated problems over a six months follow-up. No complications threatening life were reported. It is an effective method in reducing the size of the benign thyroid nodules and in controlling nodule-related compressive symptoms and cosmetic problems. RF ablation is a safe procedure and can minimize the complications could happen from surgery.

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Tables

Table 1
Pre-procedure and 1,3,6-month follow-up of patients' symptoms

		Compressive symptoms scoring (0–10)	**Cosmetic scoring (1–4)**
Pre	**Median (IQR)**	8 (6-9)	4 (3-4)
	Range	4-10	2-4
Post 1 month	**Median (IQR)**	4 (3-5)	2 (1.5-2)
	Range	2-7	1-4
Post 3 months	**Median (IQR)**	2 (1-3)	1 (1-2)
	Range	0 -5	1-4
Post 6 months	**Median (IQR)**	0 (0-1)	1 (1-1)
	Range	0-3	1-4
Test value		105.952	81.506
***P* value**		0.000	0.000
Sig.		HS	HS

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS)

Table 2
Summary of the thyroid nodule volume (ml) follow-up in the study group

		Volume (ml)	Paired t-test			
		No. = 10	Mean difference	Test value	P-value	Sig.
Pre	**Mean ± SD**	22.20 ± 4.61	-	-	-	-
	Range	16 – 30				
Post 1 month	**Mean ± SD**	12.38 ± 2.91	-9.82 ± 2.36	-13.133	0.000	HS
	Range	8.8 – 17.4				
Post 3 months	**Mean ± SD**	8.08 ± 2.92	-14.12 ± 2.82	-15.852	0.000	HS
	Range	4.4 – 12.79				
Post 6 months	**Mean ± SD**	6.90 ± 2.78	-15.30 ± 2.72	-17.786	0.000	HS
	Range	3.5 – 11.5				

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS)

Table 3
Volume reduction ratio was monitored in the study group at 1, 3, and 6 months after the procedure

Volume reduction ratio		No. = 10
Post 1 month	Mean±SD	44.27 ± 5.77
	Range	35 – 50
Post 3 months	Mean±SD	65.14 ± 8.92
	Range	55 – 77
Post 6 months	Mean±SD	71.10 ± 7.71
	Range	58 – 81

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS), •: One Way ANOVA test)

Table 4
Comparison between Echo-structure (E1, E2 and E3) according to volume (ml)

Volume (ml)		Echo-structure			Test value	P-value	Sig.
		E1	E2	E3			
		No. =	No. =	No. =			
Pre	**Mean ± SD**	26.00 ± 5.29	21.40 ± 3.51	18.50 ± 3.54	2.198	0.182	NS
	Range	2030	1726	16 – 21			
Post 1 month	**Mean ± SD**	15.47 ± 2.25	11.00 ± 2.02	11.20 ± 2.97	4.053	0.068	NS
	Range	1317.4	8.814	9.1 – 13.3			
Post 3 months	**Mean ± SD**	11.46 ± 2.14	6.40 ± 1.56	7.21 ± 2.82	6.539	0.025	S
	Range	912.79	4.48.1	5.21 – 9.2			
Post 6months	**Mean ± SD**	9.67 ± 3.18	5.50 ± 1.54	6.25 ± 2.47	3.286	0.099	NS
	Range	611.5	3.57	4.5 – 8			

Reduction ratio post 1 month	**Mean ± SD**	39.82 ± 6.04	48.69 ± 1.61	39.89 ± 4.57	6.558	0.025	S
	Range	3546.6	46.1250	36.66 – 43.12			
Reduction ratio post 3 months	**Mean ± SD**	55.79 ± 1.36	72.12 ± 5.42	61.70 ± 8.06	9.958	0.009	HS
	Range	5557.36	63.6 – 77	56 – 67.4			
Reduction ratio post 6 months	**Mean ± SD**	63.00 ± 6.25	76.80 ± 4.49	69.00 ± 2.83	7.724	0.017	S
	Range	5870	71 – 81	67 – 71			

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS), •: One Way ANOVA test

Table 5
Follow up of thyroid hormone levels (FT3, FT4, TSH) pretreatment, 1,3 and 6 months follow up

		Pre	**Post 1 month**	**Post 3 months**	**Post 6 months**
		No. = 10	**No. = 10**	**No. = 10**	**No. = 10**
FT3	Mean ± SD	2.75 ± 0.63	3.10 ± 0.39	2.85 ± 0.53	2.85 ± 0.58
	Range	2 – 3.5	2.5 – 3.5	2 – 3.5	2 – 3.5
Mean difference		--	**-0.35 ± 0.47**	**-0.10 ± 0.46**	**-0.10 ± 0.52**
Paired t-test		--	**-2.333**	**-0.688**	**-0.612**
P-value		--	**0.065**	**0.509**	**0.555**
FT4	Mean ± SD	1.17 ± 0.21	1.22 ± 0.14	1.30 ± 0.19	1.27 ± 0.24
	Range	1 – 1.5	1 – 1.4	1 – 1.5	1 – 1.5
Mean difference		--	**-0.05 ± 0.18**	**-0.13 ± 0.18**	**-0.10 ± 0.33**
Paired t-test		--	**-0.889**	**-2.327**	**-0.949**
P-value		--	**0.397**	**0.065**	**0.368**
TSH	Mean ± SD	2.70 ± 0.63	2.73 ± 0.69	2.55 ± 0.64	2.80 ± 0.67
	Range	1.5 – 3.5	1.5 – 3.5	2 – 3.5	1.5 – 3.5
Mean difference		--	**0.03 ± 0.44**	**-0.15 ± 0.47**	**0.10 ± 0.57**
Paired t-test		--	**0.213**	**-1.000**	**0.557**
P-value		--	**0.836**	**0.343**	**0.591**

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS), •: One Way ANOVA test.

Table 6
Demonstration of complications happened in the 10 patients

	Major complications	**%Of complications**	**Minor complications**	**%Of complications**
Overall complications 3 (7.5%)	Voice alterations that aren't permanent	1 (2.5%)	Hematoma	1 (2.5%)
	Rupture of the nodule	0 (0.0%)	Burning of the skin (first degree)	1 (2.5%)
	Abscess develop secondary to nodule rupture	0 (0.0%)	Vomiting	0 0 (0.0%)

Hypothyroidism	0 (0.0%)	–	–
Injury to the brachial plexus	0 (0.0%)	–	–

Figures

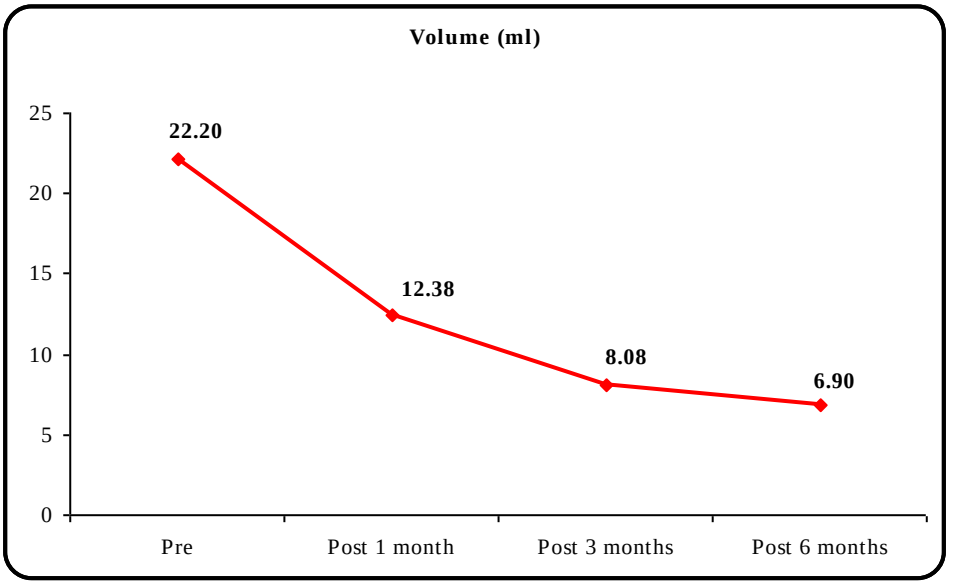

Figure 1. The line depicts the extent of the difference in volume (ml) in the study group with time.

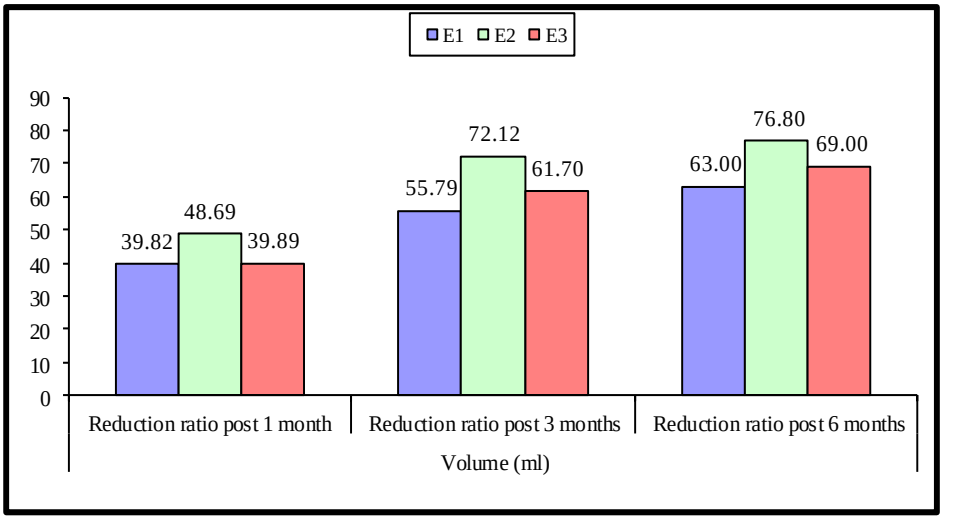

Figure 2. Relation of echo structure with volume and reduction ratio among the studied patients.

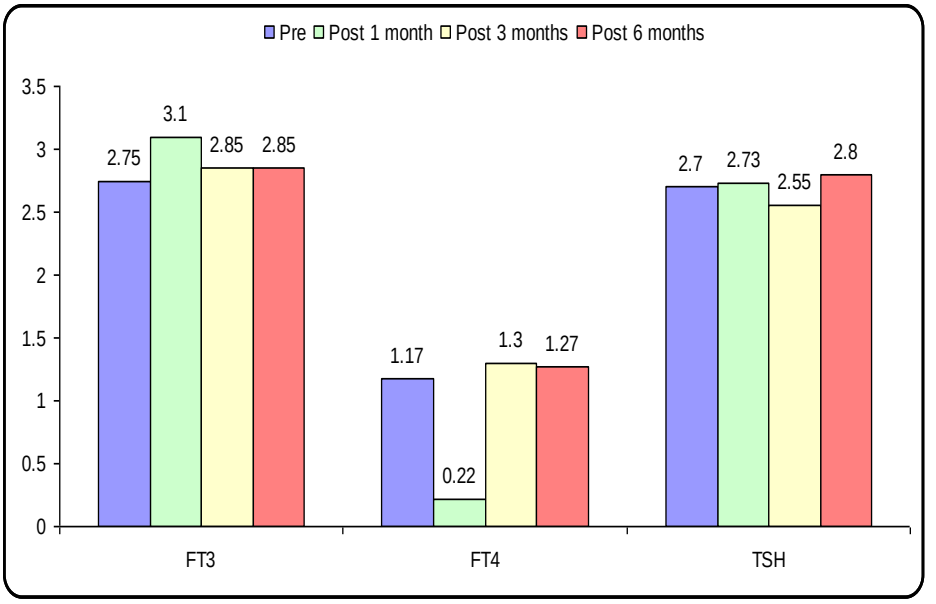

Figure 3. Hormonal parameters (FT3, FT4, TSH) follow up after 1, 3 and 6 months

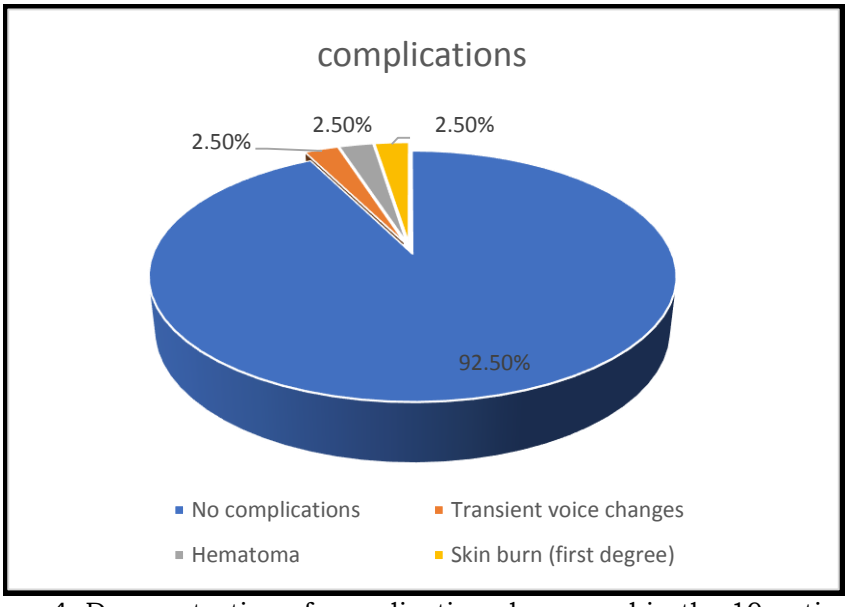

Figure 4. Demonstration of complications happened in the 10 patients.