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CLINICAL INVESTIGATION NON-VASCULAR INTERVENTIONS

Radiofrequency Ablation of Parathyroid Adenoma: Results of a Retrospective Analysis of 60 Patients

Haleh Chehrehgosha[1] · Hossein Chegini[2] · Iraj Heydari[3] · Hojat Ebrahiminik[4] · Rambod Salouti[2] · Jafar Golzarian[5]

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Abstract

Purpose To present the effectiveness and safety of radiofrequency ablation (RFA) in parathyroid adenoma (PTA).

Materials and Methods In this retrospective study, 60 patients with a single PTA were evaluated for changes in biochemical and ultrasonographic features up to 6 months after RFA of the lesion. Adenomas were ablated with an alternative technique so called "Nik jet dissection" which incorporates full hydrodissection and polar artery coagulation. Complications as well as the variations in biochemical data and nodule volumes were analyzed between baseline measurements and at each follow-up interval data (first day, 1, 3, and 6 months after ablation) were analyzed.

Results A significant reduction in serum intact parathyroid hormone and calcium levels was observed 6 months after ablation, with a mean difference of -83.4 ± 104.1 pg/mL, $p < 0.001$, and -0.29 ± 0.22 mmol/L, $p < 0.001$, respectively. Serum phosphorus levels increased significantly with a mean difference of 0.09 ± 0.19 mmol/L, $p = 0.040$ at the end of the follow up. We observed a significant volume reduction rate of parathyroid adenomas with 89 ± 20.8 percent, $p < 0.001$. Also, 51% of adenomas disappeared at the end of the follow up. In this study, two cases of hematoma and one case of transient hoarseness (grade 1 of the CIRSE classification) were encountered.

Conclusion Our study showed that RFA with the alternative technique, called "Nik jet dissection" is a safe and effective modality in management of PTA. Therefore, we suggest expanding the indications for RFA in PTA management, especially when surgery is not feasible.

Level of Evidence Level 3, Local non-random sample.

✉ Hojat Ebrahiminik
dr_ebrahiminik@yahoo.com

1 Hazrat Rasool Hospital, School of Medicine, Iran University of Medical Sciences, Tehran, Islamic Republic of Iran

2 Tirad Imaging Institute, Tehran, Iran

3 Endocrinology Research Center, Institute of Endocrinology and Metabolism, Iran University of Medical Sciences, Tehran, Islamic Republic of Iran

4 Department of Interventional Radiology and Radiation, Sciences Research Center, AJA University of Medical Sciences, Etemadzadeh St, West Fatemi St, Tehran, Tehran Province 11366, Islamic Republic of Iran

5 Radiology and Vascular Imaging, Amplatz Chair in Interventional Radiology, University of Minnesota, Minneapolis, USA

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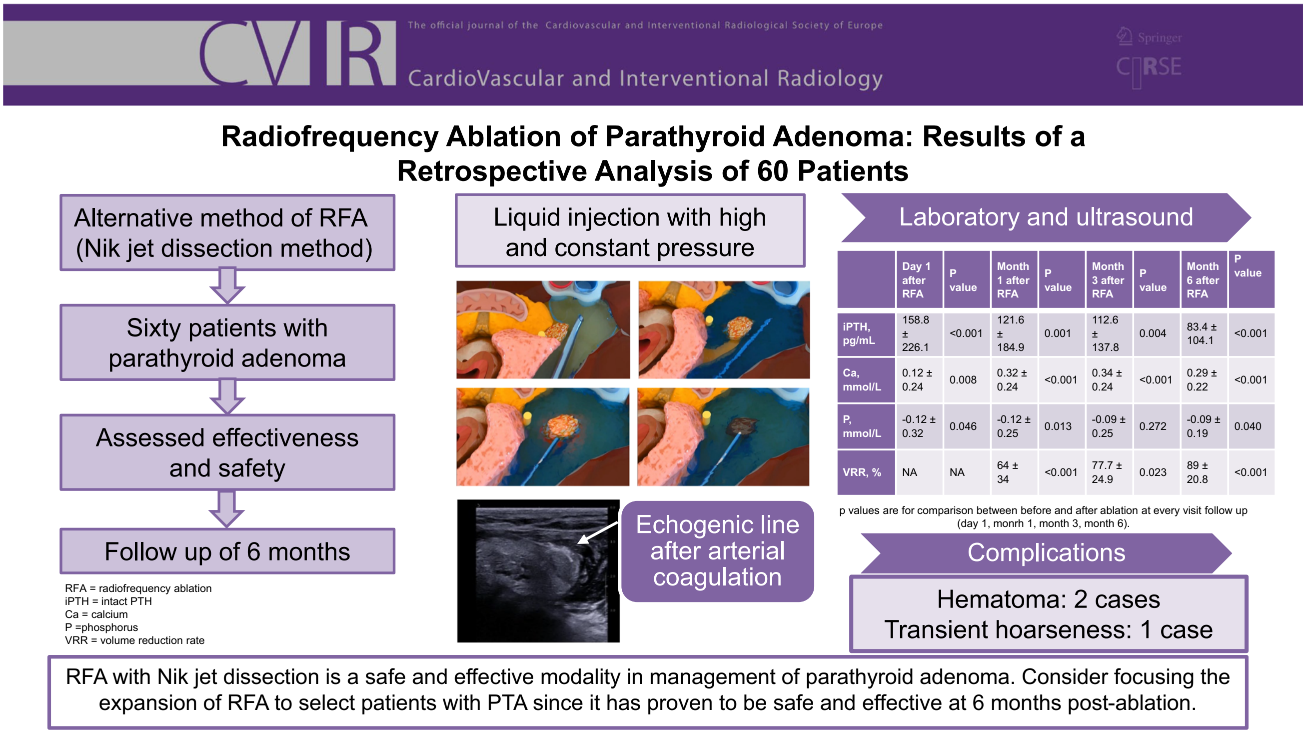
Graphical Abstract



Keywords Parathyroid adenoma · Parathyroid · Primary hyperparathyroidism · Radiofrequency ablation · Interventional ultrasonography

Introduction

Primary hyperparathyroidism (PHPT) is caused by excess secretion of parathyroid hormone (PTH) in the absence of secondary causes, with parathyroid adenoma (PTA) being the most common pathology in these patients, occurring in 80% of cases [1, 2]. PHPT can lead to serious outcomes such as fractures, nephrolithiasis, renal failure, neurocognitive impairment, cardiovascular events, and even death. Therefore, it is crucial to prevent these complications in patients with primary hyperparathyroidism [1–3].

Parathyroidectomy is the accepted treatment for PHPT, but it can result in complications such as persistent hypocalcemia, permanent hypoparathyroidism, permanent recurrent laryngeal nerve (RLN) injury (3.9%), wound infection, and hemorrhage. These complications may be increased in elderly patients with comorbidities [1, 3–5]. In recent years, radiofrequency ablation (RFA) has emerged as a promising alternative for managing parathyroid adenoma (PTA), particularly in patients who are not suitable for surgery or prefer a less invasive approach. RFA offers a rapid, outpatient procedure without the need for a surgical incision, potentially reducing the risk of complications and improving patient comfort. RFA of PTA has been shown to adequately reduce the volume of the adenomas and normalize the biochemical parameters in hyperparathyroidism [6]. Furthermore, ultrasound-guided RFA has been found to be comparable to parathyroidectomy in outcomes and complications in secondary hyperparathyroidism due to end stage renal disease [7].

This study aimed to assess the effectiveness and safety of radiofrequency ablation with an alternative method of hydrodissection, so called Nik jet dissection, in a large sample of patients with PHPT than in previous studies.

Materials and Methods

Study Population

All patients with PHPT from January 2019 to September 2023 who were referred to our center by an endocrinologist were evaluated. The diagnosis of PHPT was based on the presence of inappropriately normal or elevated PTH levels (> 65 pg/ml) in association with hypercalcemia

(> 2.52 mmol/L). Patients with PHPT were included in the study if all the following criteria were detected: 1) solitary enlarged parathyroid gland identified by preoperative ultrasonography combined with a positive sestamibi scintigraphy scan, and 2) refusal of surgery by patient or inability to tolerate general anesthesia due to comorbidities yet deemed suitable for RFA under local anesthesia setting.

Patients were precluded from this study if they have any of these criteria: 1. secondary or tertiary hyperparathyroidism, 2. suspicious malignant characteristics in sonography such as lobulation, calcification, maximum diameter > 30 mm (1), 3. technically inaccessible location such as retrotracheal, or substernal parathyroid, 4. Any evidence of parathyroid carcinoma such as serum calcium > 3.49 mmol/L, or serum PTH levels more than ten times the upper normal ranges 5. Pregnancy, 6. platelet count < 60 × 10^9/L, 8. prothrombin time > 18 s [3, 4].

Pre-procedural Assessment

Prior to ablation, ultrasound (US) was performed to evaluate and confirm visibility of the parathyroid adenoma to be targeted by ablation. Parathyroid adenoma size and features were evaluated by the same ultrasound (using "Supersonic Aixplorer® Ultimate"). Two expert radiologists with approximately 15 years of experience performed the ultrasonographic evaluation of the parathyroid glands. The volume of the parathyroid nodule was calculated by use of the ellipsoid formula (Length (cm) x Width (cm) × Thickness (cm) × π × 4/3).

Also, a sestamibi scan was performed before ablation. In cases of negative scintigraphy results or atypical features in US, or discordance between US and scintigraphy we used other modalities. For this purpose, four-dimensional (4D) CT with parathyroid protocol and fine needle aspiration (FNA) of parathyroid tissue was performed, including fluid PTH analysis (usually the result is more than ten-fold exceeding than serum levels of PTH).

The Radiofrequency Ablation Technique

The patient was placed supine with their neck extended. First, 2–5 mL of 2% lidocaine was administered subcutaneously for local anesthesia. Next, for hydrodissection a 19 gauge lumbar puncture needle was inserted into the target points usually on the inferomedial side of the adenoma. In certain instances, we utilized other sides of the adenoma, such as lateral, or cephalocaudal, to improve the intervention. Then, 50–100 mL of cold 5% dextrose in water was injected with constant pressure to separate the adenoma from neighboring structures such as esophagus, trachea, major vessels, visible nerve structures such as vagus nerve, sympathetic ganglion, cervical spinal nerve, and probable pathway of recurrent laryngeal nerve such as tracheoesophageal groove. This high and constant pressure was applied by aiding the pressure of the thumb behind the syringe. This pressure was performed simultaneously with needle movement in target tissue; so, the pressure of the outgoing fluid would be positive, and it resulted in the wide distance between needle tip and target tissue.

After full dissection (dissection of 360 degrees around the lesion with a distance of about one cm from vital surrounding organs as mentioned above), an RFA electrode (5–7 mm active tip) was placed in the PTA. We started ablation at the perfusion center (polar artery) of the adenoma with a high watt (near > 75 W), considering the special vascularity of the parathyroid. Then, the usual formal moving-shot technique was used to ablate different parts of the lesion after artery thrombosis (Figs. 1, 2).

In this study, we used an alternative hydrodissection technique that we named "Nik jet dissection" in all patients. Desired hydrodissection around PTA was carried out with 5–7 mm active tip RF electrode and a system watt of 25 to ~ 75 watts for artery coagulation and tissue ablation. This technique was named after the name of the innovator author, explained in video 1.

Outcome Measures and Follow-up

The patients were followed up for a period of 6 months, during which serum intact PTH (iPTH), calcium, and phosphate levels and size of adenoma were measured. Also, any complications such as hoarseness, local infection, and symptoms of hypocalcemia were assessed during the follow-ups. Close monitoring of patients for any loss of consciousness, voice abnormality, and hemodynamic instability was performed during ablation. We reported any complications after ablation regarding to Cardiovascular and Interventional Radiology Society of Europe (CIRSE) classification.

Statistical Analysis

All data were analyzed using SPSS 23.0.0 software (IBM, Chicago, IL). Baseline characteristics were reported as percentages for categorical variables and means ± standard deviation (SD) for continuous variables. Comparisons of outcome measures were analyzed with paired *t*-tests or paired Wilcoxon rank tests and the significant levels were reported when $p < 0.05$.

Results

A total of 60 patients were incorporated in our study, and 47 (79.7%) patients were female. The mean age of the patients was 60.7 ± 12.6 years, and the mean volume of

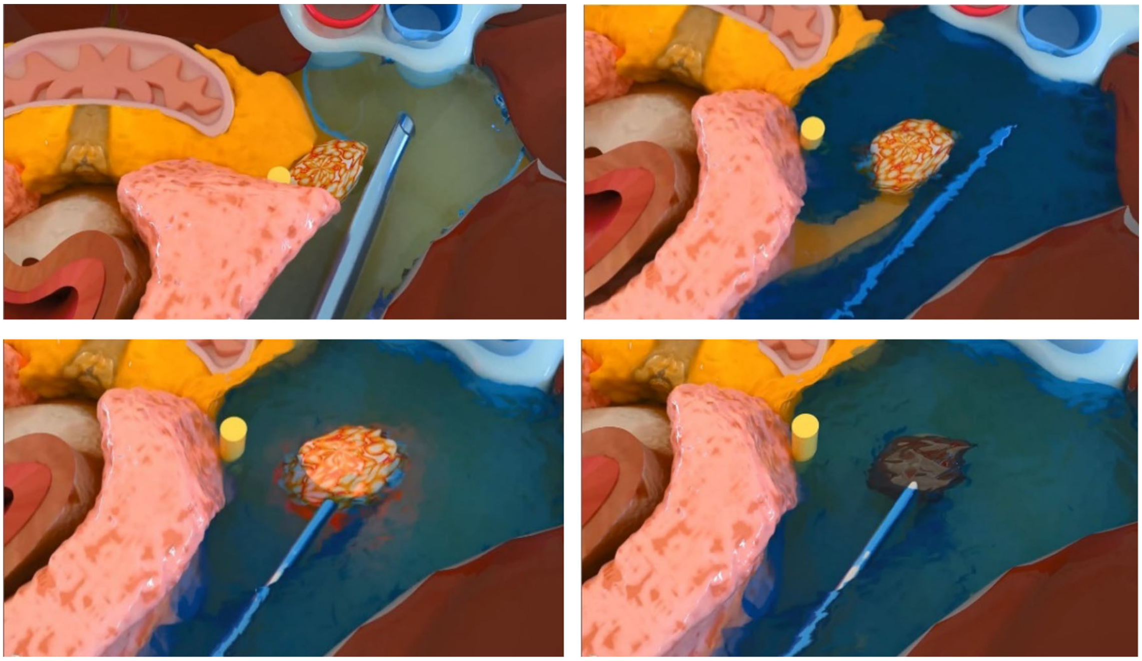


Fig. 1 Nik Jet dissection method. Liquid injection with high and constant pressure starting in the area adjacent to the target tissue to perform dissection. It has some advantages: **1.** less damage during the movement of the needle due to the presence of fluid pressure between the sharp tip of the needle and the adjacent tissues. **2.** controlling the direction of the dissection by targeted rotation of the needle's beveled gap. **3.** more probability of liquid entrance to the intended potential space between target tissue and its surrounding tissue in a more safe and effective way by creating liquid pressure. **4.** non-occlusion of the needle lumen by tissue particles and clots due to the liquid pressure

PTA was 5.1 ± 4.9 mL with a range of 0.2–20.4 mL. The mean maximum diameter of the nodules was 14.3 ± 5.2 mm (5.8–25.0 mm). The baseline demographic, clinical, and laboratory data of the patients are shown in Table 1. Out of forty-seven patients who underwent sestamibi scintigraphy, adenomas were detected in 42 (89.3%) of them. Also, the US revealed five (10%) adenomas that were not visible in scintigraphy. The location of the nodules detected was different between the scintigraphy and the US in 7 (16%) positive scintigraphy adenomas. The most frequent location of the parathyroid adenoma that was detected in ultrasonography was the lower pole of the thyroid with a frequency of 87% (Fig. 3).

Laboratory Data

One day after ablation, there was a significant reduction ($p < 0.001$) in iPTH levels (155.3 ± 114.4 to 35.7 ± 46.1 pg/ml). Serum calcium levels were significantly reduced from 2.66 ± 0.22 to 2.52 ± 0.27 mmol/L ($P = 0.0$ 08) immediately after ablation. After 6 months, serum iPTH and calcium levels were significantly decreased from 155.3 ± 114.4 pg/ml at baseline to 76.2 ± 45.9 pg/ml ($p < 0.001$), and from 2.66 ± 0.22 mmol/L at baseline to 2.37 ± 0.14 mmol/L ($p < 0.001$), respectively. There was a significant rate of hyperparathyroidism cure (serum calcium level ≤ 10.2) after 6 months. Serum phosphorus levels were significantly increased after one day ($p < 0.046$), 1 month ($p < 0.013$) and 6 months ($p < 0.040$) in comparison with baseline levels. While the changes in serum phosphorus levels were not statistically significant at 3 months after ablation ($p = 0.272$). All data and differences of iPTH, calcium, and phosphate levels from baseline are shown in Table 2 and 3.

We observed that serum calcium levels showed a significant decrease ($p = 0.007$) at one month and ($p = 0.018$) at 6 months in comparison to the baseline level. However, this decrease was not significant at 3 months in comparison with first day level ($p = 0.187$). The same pattern was shown for iPTH levels when compared to the first day ($p < 0.001$) in months 1 and 6 but not significant when compared with 3 months after ablation. There were not any significant changes in phosphate levels during the follow-up, compared to the baseline (Fig. 4).

In addition, there was not a significant change in 25-hydroxy vitamin D (84.61 ± 26.48 to 89.6 ± 6.48 nmol/L, $p = 0.645$), alkaline phosphatase (170.8 ± 72.5 to 131.8 ± 59.8 IU/L, $p = 0.241$), glomerular filtration rate (GFR) (70.4 ± 14.6 to 70.6 ± 14.1 ml/min/1.73 m^2, $p = 0.939$), 24 h urinary calcium (112.5 ± 3.5 to 58 ± 39.6 mg/24 h, $p = 0.325$), TSH (2.5 ± 1.3 2.7 ± 2 mIU/L, $p = 0.80$), and T4 (77.23 ± 1.28 105.55 ± 21.88 nmol/L, $p = 0.295$).

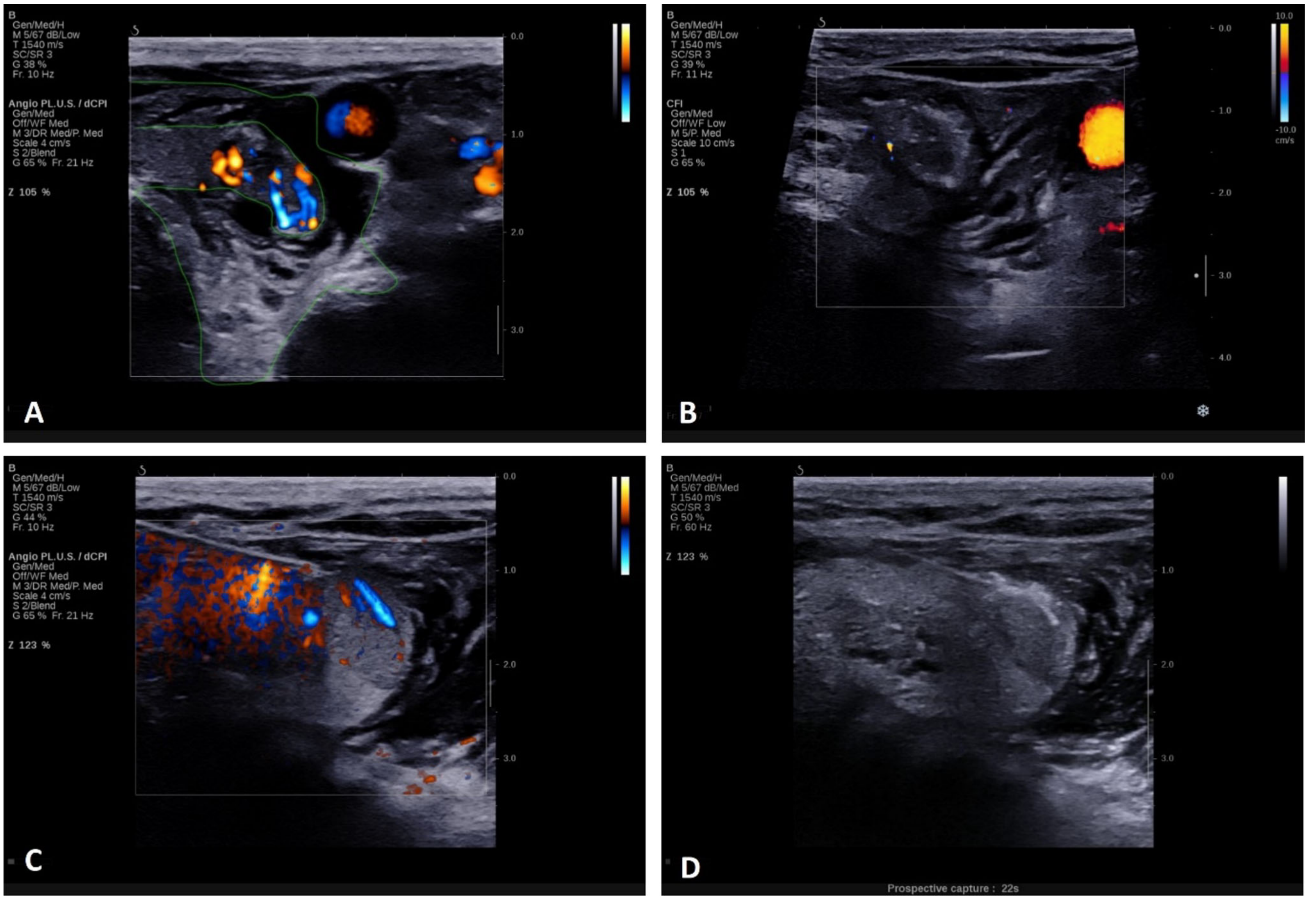


Fig. 2 Ultrasonographic features of radiofrequency ablation (RFA). **A.** Sonography features showed full dissection method and hypervascular parathyroid adenoma (PTA) before RFA. **B.** Avascular PTA with echogenic rim after RFA. **C.** Targeted polar artery before arterial coagulation. **D.** Linear echogenic area after arterial coagulation

Ultrasound Data

The PTA volume significantly decreased from 5.1 ± 4.9 mL at baseline to 1.9 ± 2 mL at one month ($p < 0.001$), 1.1 ± 1.8 mL at 3 months ($p = 0.023$), and 0.4 ± 0.7 mL ($p < 0.001$) at 6 months after ablation. The volume reduction rate of the PTA in comparison with preprocedural data was 64 ± 34 percent, 77.7 ± 24.9 percent, and 89 ± 20.8 percent respectively at 1, 3, and 6 months after RF ablation. The parathyroid nodules were undetectable in 51% of cases 6 months after the RF ablation.

Parathyroid ultrasonography detected hypoechogenicity in 74.6%, heteroechogenicity in 22%, and hyperechogenicity in 3.4% of PTAs before RF ablation. After ablation, all the nodules showed hypoechogenicity. Also, they had a typical vascularity pattern in 94.9% of cases before ablation, which changed to avascularity after RF ablation.

Complications

According to CIRSE classification, we observed 3 cases of grade 1 complication. Two cases of hematoma and one case of transient hoarseness disappeared immediately after the injection of cold dextrose water around the ablated adenoma prior to the end of the procedure of ablation. No patient had severe hypocalcemia or needed hospitalization after the procedure.

Discussion

We found that serum calcium and iPTH levels and size of the adenoma decreased significantly during the 6-month after RFA. In this regard, there are some case reports that showed normalization of serum PTH levels and disappearance of the PTA after RFA [2, 7]. Wei et al. evaluated and compared the effectiveness and safety of RFA. They showed 94.6% reduction rate of the adenoma at 12 months. However, RFA was applied only in 23 patients in this study [3]. The same results were reported in another study with 27 patients (4). This is while our study is larger than previous studies, and we used Nik jet dissection technique that can result in both vascular and cellular ablation due to thermal effect of RFA. The increased zone of ablation along with initial artery coagulation in our technique, may offer several advantages: (1) Improvement of accessibility

Table 1 Characteristics of the patients at baseline

Characteristic	Data
Sex (female)	47 (79.7%)
Age (years)	60.7 (12.6)
Ischemic heart disease	8 (13.6%)
Hypertension	16 (27.1%)
Diabetes mellitus	10 (17.0%)
Hypothyroidism	7 (11.9%)
Nephrolithiasis	3 (5.0%)
Osteoporosis	12 (20.0%)
Parathyroid surgery	5 (8.3%)
iPTH (pg/mL)	155.3 ± 114.4
Serum calcium (mmol/L)	2.66 ± 0.22
Serum phosphorus (mmol/L)	1 ± 0.19
Alkaline phosphatase (IU/L)	168.7 ± 61.8
25-hydroxy Vitamin D (nmol/L)	84.61 ± 26.48
Serum TSH (mIU/L)	2.5 ± 1.4
Serum T4 (nmol/L)	77.23 ± 1.28
GFR (mL/min/1.73 m^2)	67.9 ± 24.5
Urinary calcium (mg/24 h)	262.9 ± 176.7

Data are listed as mean ± SD for normally distributed parameters or n (%) *iPTH*Intact parathyroid hormone, *GFR* Glomerular filtration rate, *TSH* Thyroid stimulating hormone

to the parathyroid lesion due to a wider field of operation. (2) The lower rate of angiogenesis and parathyromatosis (non-intended seeding during the procedure) which was prevented by fat ablation around the adenoma. (3) A lower probability of recurrence rate due to better visibility of the lesion and less intraoperative bleeding.

In accordance to previous studies [4, 8], serum iPTH was increased after 3 months of follow-up and then decreased in month 6 in our study. Although this phenomenon is an unclear point in this context, it was also reported after parathyroidectomy [9]. One hypothesis for this increased secretion of iPTH is removal of the suppression of the other normal parathyroid glands after RFA. Confirming the findings from other studies [4, 8], we showed that this elevated iPTH does not affect calcium levels or other clinical outcomes in the third month of the follow-up. This point is according to the recommendation of surgical guidelines that serum calcium levels should be measured instead of iPTH levels due to variability in serum levels and unpredictability of iPTH in follow-up [4].

In contrast with another study [4], there was an increase in serum phosphate levels during follow up. It seems that the role of serum phosphate is still debatable in monitoring of hyperparathyroidism.

We did not observe any cases of severe and symptomatic hypocalcemia. A few hypotheses can be discussed; Firstly, severe hyperparathyroidism (calcium above 3.49 mmol/L) was not eligible for RFA due to high probability of the parathyroid carcinoma, so we did not observe hungry bone syndrome. The second one was the role of other parathyroid glands in the maintenance of serum calcium levels; Normal parathyroid glands were not affected during ablation. Safety of RFA of parathyroid adenoma has been already addressed in previous studies [1–4, 6–19]. In this regard, Wei et al. reported complication rates of only

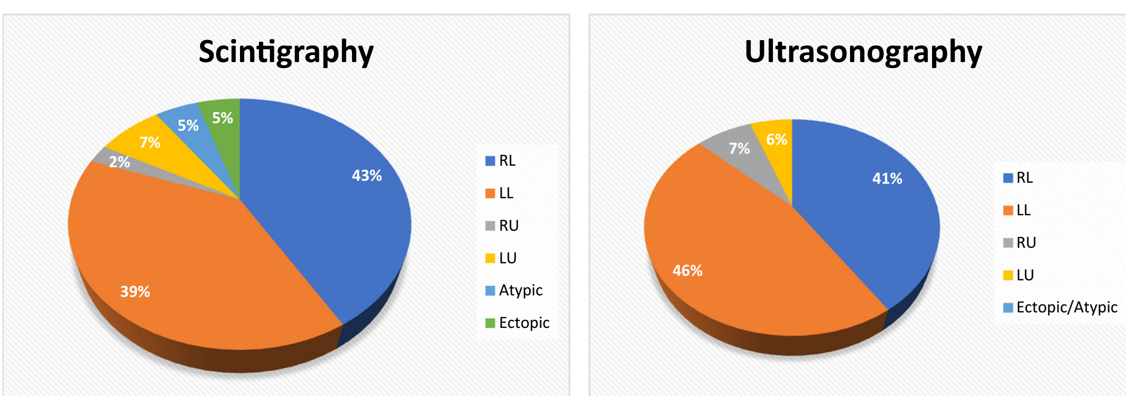


Fig. 3 Localization of parathyroid adenoma (PTA) by ultrasonography and sestamibi scintigraphy. **Left.** Results of the sestamibi scintigraphy before radiofrequency ablation (RFA). **Right.** Data of the parathyroid ultrasonography before RFA. RL = Right lower parathyroid, LL = left lower parathyroid, LU = left upper parathyroid, RU = right upper parathyroid. Regarding the location of the adenoma according to scintigraphy and ultrasonography, the most frequent involvements were related to the RL parathyroid and LL parathyroid respectively. The lower pole of thyroid was the most common site (79.7%) of PTA according to Ultrasonography

Table 2 Serum levels of iPTH, calcium, and phosphorus, and volume of the adenoma during the follow up

	Before ablation	Day 1 after ablation	Month 1 after ablation	Month 3 after ablation	Month 6 after ablation
iPTH, pg/ml	155.3 ± 114.4 (39.8–645)	35.7 ± 46.1 (3–236)	66.5 ± 53.3 (3–266)	79.0 ± 61.8 (10.4–285)	76.2 ± 45.9 (11.6–234)
Calcium, mmol/L	2.66 ± 0.22 (2.22–3.24)	2.52 ± 0.27 (1.79–3.11)	2.37 ± 0.17 (1.84–2.79)	2.37 ± 0.14 (2.09–10.7)	2.37 ± 0.14 (2.02–2.74)
Phosphorus, mmol/L	1 ± 0.19 (0.67–1.7)	1.12 ± 0.22 (0.61–1.48)	1.09 ± 0.12 (0.8–1.41)	1.09 ± 0.12 (0.9–1.35)	1.09 ± 0.12 (0.8–1.35)
Volume, mL	5.1 ± 4.9 (0.2–20.4)	NA	1.9 ± 2 (0–7.5)	1.1 ± 1.8 (0–7.5)	0.4 ± 0.7 (0–3.1)

Data expressed as mean ± SD for normally distributed parameters and lower and upper data range were shown on the parenthesis

Table 3 Changes in volume of the PTA and serum levels of iPTH, calcium, and phosphorus and PTA volume

	Day 1 after ablation	P^*	Month 1 after ablation	$P^†$	Month 3 after ablation	$P^‡$	Month 6 after ablation	$P^§$
iPTH changes, pg/mL	158.8 ± 226.1 (− 21, 1249)	**< 0.001**	121.6 ± 184.9 (− 74.3, 1028)	**0.001**	112.6 ± 137.8 (− 70.4, 519)	**0.004**	(− 47.6, 411)	**< 0.001**
Calcium changes, mmol/L	0.12 ± 0.24 (− 0.39, 0.64)	**0.008**	0.32 ± 0.24 (− 0.17, 0.84)	**< 0.001**	0.34 ± 0.24 (− 0.32, 0.79)	**< 0.001**	0.29 ± 0.22 (− 0.04, 0.84)	**< 0.001**
Phosphorus changes, mmol/L	− 0.12 ± 0.32 (− 0.67, 0.74)	**0.046**	− 0.12 ± 0.25 (− 0.61, 0.87)	**0.013**	− 0.09 ± 0.25 (− 0.45, 0.61)	0.272	− 0.09 ± 0.19 (− 0.45, 0.19)	**0.040**
VRR, %	NA	NA	64 ± 34 (− 69.9, − 100)	**< 0.001**	77.7 ± 24.9 (1.8, − 100)	**0.023**	89 ± 20.8 (0, − 100)	**< 0.001**

Continuous variables expressed as means ± standard deviation (SD) with lower and upper limit of data on parenthesis. Categorical variables expressed as percentages. Changes were calculated with pre-ablation data minus post-ablation data. p = p value and statistically significant p values ($p < 0.05$) are in bold. * = p value between before and after ablation at day one, † = p value between before and after ablation at month one, ‡ = p value between before and after ablation at month three, § = p value between before and after ablation at month six

iPTH, Intact parathyroid hormone; VRR, Volume reduction rate of the nodule (pre-ablation volume-post-ablation volume/pre-ablation volume × 100); NA, Not applicable

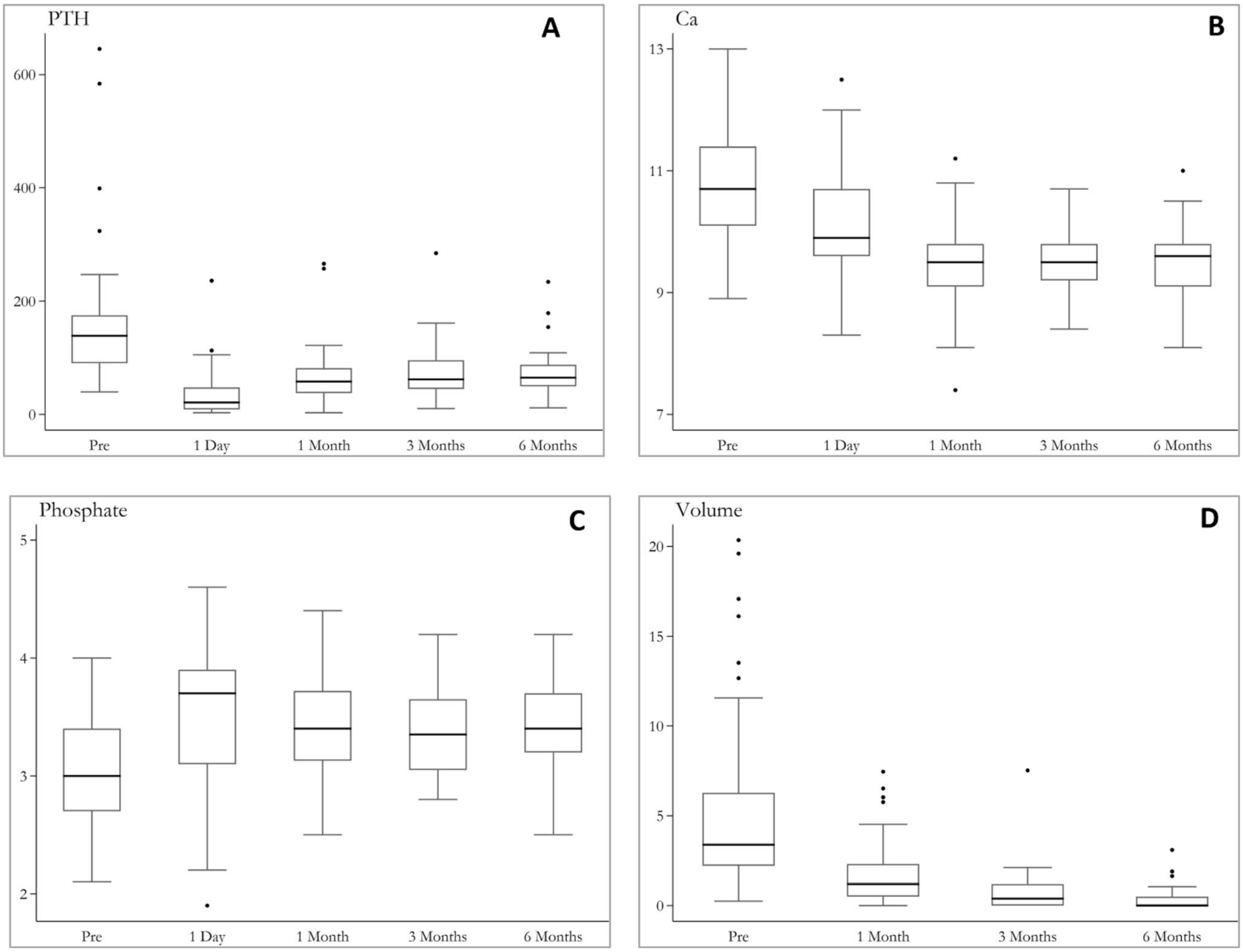


Fig. 4 Box and whiskers diagrams of serum intact parathyroid hormone (iPTH), calcium, phosphate, and volume of parathyroid adenoma (PTA). Box and whiskers diagrams. **A.** Serum iPTH (pg/mL), **B.** Serum calcium (mg/dl), **C.** Phosphate (mg/dl), and **D.** Volume of PTA (mL) before and after radiofrequency ablation. Pre = pre-ablation

6.7% after RF ablation and detected only one case of persistent voice impairment [3]. It is important to mention that complication rates were lower than results of the other studies that applied RFA of the parathyroid adenoma. This can be due to the method of extensive hydrodissection that was applied in this study.

There are a few limitations to our study. This is a retrospective study, and follow-up was limited to 6 months. Another limitation is the lack of a control group; however, this study has a larger sample size than the previous studies in this field and we observed a significant improvement during this 6-month follow-up.

In conclusion, this study showed that RF ablation with Nik jet dissection and polar artery coagulation is a safe and effective modality in management of parathyroid adenoma. It does not need hospitalization and general anesthesia. Based on the results of this study we suggest that RFA in selected patients with symptomatic parathyroid adenoma using the so-called Nik jet dissection is safe and effective at 6 months post-ablation. A randomized, prospective trial comparing RFA with parathyroidectomy may provide more information about which patients will benefit from each technique.

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Declarations

Conflict of interest The authors declare that they have no conflict of interest.

Ethical Approval This retrospective study was endorsed by the Ethics Committee of Iran University of Medical Sciences (ethics code.R.IUMS.FMD.REC.1401.1050) and was consonant with the principles of the Declaration of Helsinki.

Informed Consent Written informed consent was obtained from all patients before RF ablation.

Consent for Publication For this type of study consent for publication is not required.

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