Original Article

Radiofrequency Ablation of Parathyroid Adenomas: Safety and Efficacy in a Study of 10 Patients

Anubhav Harish Khandelwal, Smarth Batra, Surabhi Jajodia, Saurabh Gupta, Rohit Khandelwal, Abhay Kumar Kapoor, Sunil Kumar Mishra[1], S. S. Baijal

Departments of Interventional Radiology and [1]Endocrinology and Metabolism, Medanta-The Medicity, Gurugram, Haryana, India

Abstract

Purpose: To evaluate safety and effectiveness of ultrasound-guided percutaneous radiofrequency ablation of parathyroid adenoma in surgically unfit patients with hypercalcemia because of hyperparathyroidism. **Materials and Methods:** A retrospective review of hospital records from Jan 2012 to Dec 2018 revealed 10 patients, who had undergone ablation for solitary parathyroid adenoma. All 10 patients suffered from hyperparathyroidism because of parathyroid adenoma, resulting in hypercalcemia. These patients were surgically unfit because of comorbidities. Pre-ablation serum calcium and serum parathormone levels were measured and compared with the levels after the ablation. **Results:** Mean serum calcium level decreased significantly from 2.81 ± 0.17 mmol/L pre-ablation to 2.42 ± 0.17 mmol/L 72 h after ablation and parathyroid hormone levels became normal in all patients within 7 days. Seven patients remained normo-calcaemic at 6 months follow-up with no signs and symptoms of hyperparathyroidism. One patient with pancreatitis died after 15 days because of pre-existing multi-organ failure. Two patients were lost to follow-up before 6 months. **Conclusion:** Radiofrequency ablation of parathyroid adenoma is a safe and effective alternate treatment method for symptomatic hypercalcemia in surgically unfit patients suffering from primary hyperparathyroidism because of parathyroid adenoma.

Keywords: Hypesrcalcemia, hyperparathyroidism, parathyroid adenoma, radiofrequency ablation

Introduction

Primary hyperparathyroidism is associated with elevated levels of serum calcium because of over secretion of parathormone.[1] The incidence of primary hyperparathyroidism in the USA has been reported to range from 0.7% in the general population up to 3% in postmenopausal women.[2-4] Parathyroid adenomas are the most common cause for primary hyperparathyroidism with an incidence of 80--85%.[5] Standard method of treatment for a parathyroid adenomas causing hyperparathyroidism is parathyroidectomy.[6] Previous studies have shown that parathyroidectomy for primary hyperparathyroidism is curative in greater than 95% of cases when performed by an experienced surgeon.[7] Although it is curative, the need for general anesthesia in patients having comorbidities may not always make them suitable to undergo surgical procedure. Also, the consequences of having a post-surgical scar and possible risk for life-long hypoparathyroidism may make some patients not wanting to undergo surgery. A few authors do endorse use of minimally invasive parathyroid surgery using local instead of general anesthesia.[8-10] However, limitations including lack of compliance in some patients, inadequate skill, concomitant thyroiditis, recurrent laryngeal nerve palsy, wound infection, intraoperative hemorrhage and a resultant conversion of procedure to general anesthesia in 10% of cases, needs consideration.[11,12] Hence in such patients and patients with comorbidities, minimally invasive non-surgical treatment methods serve a viable option.

Use of non-surgical techniques of ethanol ablation and radiofrequency ablation for treatment of parathyroid adenoma have shown to yield good clinical results.[13-15]

Radiofrequency ablation (RFA) is a minimally invasive technique that has been used to treat benign nodules of the thyroid[16] and para-thyroid glands.[17,18] In 2017, the Korean

Access this article online

Quick Response Code:

Website: www.ijem.in

DOI: 10.4103/ijem.IJEM_671_20

Address for correspondence: Dr. Anubhav Harish Khandelwal, Department of Interventional Radiology, Medanta-The Medicity, Gurugram, Haryana, India.
E-mail: anubhav1703@gmail.com

Submitted: 05-Oct-2020 **Revised:** 18-Nov-2020
Accepted: 16-Dec-2020 **Published**: 12-Jan-2021

How to cite this article: Khandelwal AH, Batra S, Jajodia S, Gupta S, Khandelwal R, Kapoor AK, *et al*. Radiofrequency ablation of parathyroid adenomas: Safety and efficacy in a study of 10 patients. Indian J Endocr Metab 2020;24:543-50.

Society of Thyroid Radiology proposed the new guidelines for RFA in benign thyroid nodules and recurrent thyroid cancers.[19] They strongly recommended RFA as a first line treatment for symptomatic or cosmetically problematic, solid or predominantly solid, histologically proven benign thyroid nodules including toxic or pre toxic autonomously functioning thyroid nodules (AFTN). RFA was also strongly recommended treatment for curative or palliative purposes in recurrent thyroid cancers at thyroidectomy bed and cervical lymph nodes for patients with high surgical risk or patients who refuse surgical treatment.

The more recently published European Thyroid Association Guidelines[20] and Consensus Statement from the Italian minimally invasive treatments of the thyroid (MITT) group, are in accordance with the Korean guidelines for treating benign thyroid nodules and they recommend that in cases of benign non-functioning multinodular goiter, thermal ablation with RFA should be considered only in patients who refuse or are not fit for surgical treatment.[21]

Likewise RFA has also been used to treat hyperfunctioning adenomas of parathyroid gland in various case reports.[17,18] However, there is still paucity of published literature with no definitive standard guidelines for non-surgical treatment of parathyroid gland adenomas. The management decisions have to be truly based on evidence from case reports and small case series.

The current study is the largest single center experience evaluating the role of radiofrequency ablation in the treatment of parathyroid adenomas.

Materials and Methods

The protocol of this study was approved by the Ethics Committees of the Institutional Review Boards. Written informed consent was obtained from all patients before they underwent RFA.

From Jan 2012 to Dec 2018, 10 patients (6 male and 4 female) aged 36--73 years (mean age of 55.2 years) were considered for minimally invasive treatment for solitary parathyroid adenoma causing hyperparathyroidism and hypercalcemia, at a tertiary care hospital in North India. Diagnosis and localization of a solitary adenoma of parathyroid gland in all these 10 patients were made on 99mTc Sestamibi scan and ultrasound examination. RFA was the modality used for minimally invasive treatment of solitary parathyroid adenomas. RFA in all patients were carried out by interventional radiologists. First author was the primary operator for last 8 patients while procedure in first two patients was performed by the last author with first author being the first assistant.

A pre-ablation, surgical consultation was taken in all patients. The comorbidities, which deemed these patients unfit for surgery were chronic liver disease (CLD) in 5 patients [one of which had hepatocellular carcinoma and three patients with liver failure awaiting living donor liver transplantation (LDLT)], chronic kidney disease (CKD) in 2 patients [one of which had additional coexisting chronic obstructive Pulmonary Disease (COPD)], acute severe necrotising pancreatitis in 2 patients and subacute intestinal obstruction with dilated cardiomyopathy and low ejection fraction in 1 patient. [Table 1]. The patients with acute severe necrotising pancreatitis (two patients), patients requiring LDLT for liver failure (three patients) and the patient with subacute intestinal obstruction (one patient) were pre-admitted for treatment of these comorbidities while the remaining four were admitted in day care for the ablation. All the 10 patients were on medical management.

The pre-procedural evaluation included serum calcium levels, serum parathormone levels, complete blood count, and blood coagulation tests (prothrombin time, activated partial thromboplastin time and INR) in all 10 patients. The post-procedure evaluation strategy was monitoring serum calcium levels 72 h post-procedure and serum parathyroid hormone levels after 7 days. Vitamin D levels were only available for 4 patients in pre-procedure period and were within normal range. Post-procedure evaluation was however not available for any patient in our study.

Patients were counselled regarding the procedure and need for analgesics, in case they encountered pain in the post-procedure period. After informed consent, parathyroid adenomas in all patients were evaluated for size, echotexture, and vascularity with an ultrasound machine [Figure 1] using a 5--10 MHz linear transducer (Acuson Antares, Siemens Medical Solutions USA, Inc., Mountain View, CA 94043 U.S.A) and a plan was made for safe electrode deployment to achieve effective ablation using a 17G internally cooled monopolar electrode with a 5 mm active tip (VIVA RF Electrode, STARmed Co., Ltd., Gyenonggi-do, Korea), connected to a radiofrequency generator (VIVA RF Generator, STARmed Co., Ltd., Gyenonggi-do, Korea) using an output of 40W--80W energy.

Procedure

Procedure was performed after securing a peripheral intravenous access. All patients were placed in the supine position with the neck extended, by keeping a positioning cushion under the shoulder. Grounding pads were fixed to both thighs. All patients underwent ablation after injecting

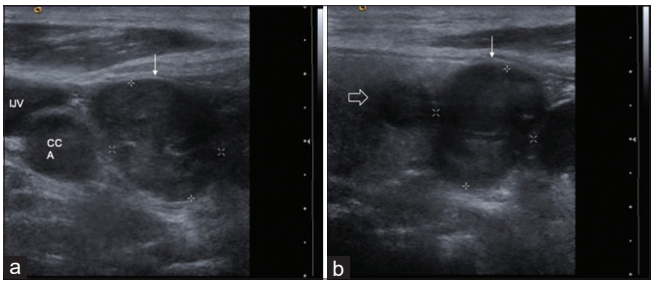

Figure 1: (a) Transverse ultrasound scan of right side of neck showing a large right sided inferior parathyroid adenoma (arrow). (b) Longitudinal ultrasound scan of right neck showing right inferior parathyroid adenoma (arrow) and a small thyroid nodule (open arrow). Abbreviation: CCA = Common carotid artery, IJV = Internal Jugular Vein

Table 1: Patient characteristics and associated comorbidities

Patient Number	Gender	Age (in years)	Comorbidities
1	Female	36	Chronic Kidney Disease
2	Male	59	Chronic Liver disease awaiting Liver Transplantation
3	Male	66	Chronic Liver disease awaiting Liver Transplantation
4	Female	72	Sub-acute intestinal obstruction with dilated cardiomyopathy and atrial fibrillation.
5	Male	44	Acute Pancreatitis
6	Female	58	Chronic Liver Disease
7	Male	38	Chronic Liver disease awaiting Liver Transplantation
8	Male	73	Chronic Liver disease with Hepatocellular carcinoma
9	Male	68	Chronic Kidney disease with chronic obstructive pulmonary disease
10	Female	38	Acute Pancreatitis

2% lidocaine at the puncture site and around the para-thyroid gland in direct approach and up to the thyroid capsule in trans-thyroidal approach. Two patients were pre-intubated because of their comorbid condition. Skin incision was not required in any patients for assisting insertion of the RF electrode. Two different approach routes were taken for electrode placement [Figure 2]; a direct approach in 3 patients where the adenomas were large and projecting lateral to thyroid and a trans-thyroidal approach in 7 patients where adenomas were small and underlying the thyroid gland. Care was taken to avoid the vessels along the approach route guided by color Doppler ultrasound. The electrode tip was positioned in the deepest and most medial and distal portion of the parathyroid adenoma. Ablation was initiated at 40W and was carried out using "moving shot" technique.[22] The energy was reduced to 20–30 Watts if patient complained of intolerable pain. When a transient echogenic cloud, representing small zone of ablation, appeared around the electrode tip (on an average within 3--5 s), it was moved proximally in a non-ablated part of adenoma. This step was repeated in a way as to cover the entire nodule with echogenic cloud of ablation [Figure 3].

Hydro-dissection was carried out in one patient by instilling 10 ml of 5% dextrose between the common carotid artery and the adenoma, to obviate the heat sink effect Figure 4).

The technical end point of ablation was coverage of entire adenoma with an echogenic cloud and absence of colour flow on Doppler ultrasound exam within the ablated nodule after disappearance of echoes.

Post-procedure patients were monitored for 3 hours for any procedure related complications.

Results

Five patients (50%) had adenomas in the left inferior parathyroid gland, three patients (30%) in right inferior parathyroid gland, and two in right superior parathyroid gland (20%). Size of these adenomas ranged from 9 mm to 35 mm in their longest dimension [Table 2].

Safe targeting and complete ablation of the parathyroid adenomas was achieved in all 10 patients (100%).

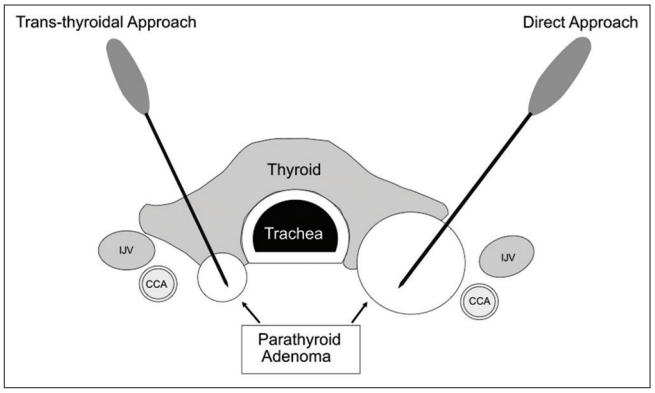

Figure 2: Diagrammatic representation of two different types of approach to placement of RFA electrode into parathyroid adenoma for percutaneous ablation; Trans-thyroidal and Direct approach

No patient required any post-procedure analgesia. 4 out of 10 patients who got admitted electively for the procedure were discharged from hospital the same day and with advice to get serum calcium levels checked after 72 h and parathyroid hormone levels after 7 days.

The immediate postoperative period in 9 of the 10 patients who underwent procedure was uneventful. The only complication was hoarseness of voice encountered in one of the patients, which resolved spontaneously within 3 weeks.

Serum parathyroid hormone levels and serum calcium levels normalized in the postoperative period. Serum calcium levels normalized within 72 h in all patients [Table 3a]. Mean Serum calcium levels fell from 2.81 ± 0.17 mmol/L (ranging from 2.59 to 3.14 mmol/L) to 2.42 ± 0.12 mmol/L (ranging from 2.1 to 2.54 mmol/L). The elevated pre-procedure parathyroid Hormone levels (ranging from 181.7 ng/L to 10148.5 ng/L) became normal in all patients within a week [Table 3b].

One patient died of multi-organ failure because of underlying severe acute necrotizing pancreatitis, 15 days post-procedure.

At 6 months of follow-up 7 out 9 patients (Two patients were lost to follow-up in the early post-procedure period) remained normocalcemic with no signs and symptoms of hypo or hyperparathyroidism. Out of these 7 patients, two patients were lost to follow-up after their first 6-month

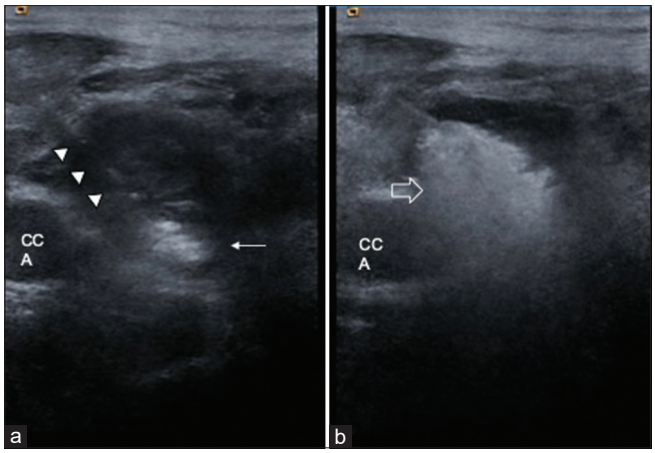

Figure 3: (a) RFA electrode (arrow heads) placed via direct approach into the right inferior parathyroid adenoma, Echogenic cloud of ablation around the tip of electrode (Arrow). (b) Echogenic cloud from ablation covering the entire adenoma (open arrow). Abbreviation: CCA = Common carotid artery

outpatient visit. Two more patients were lost to follow-up after hospital visits at 12 months and 18 months, respectively, both being asymptomatic and normocalcemic [Tables 3a and b]. One patient died at 20 months and another after 7 years post-procedure because of unrelated causes but remained asymptomatic for hyperparathyroidism till their demise, as per retrospective telephonic interview with their families. One patient maintains follow-up as an outpatient and has completed 29 months being free from symptoms of hyper or hypoparathyroidism and has normal lab parameters. Imaging to record size change of parathyroid adenomas was not used as a parameter for follow-up and was planned to be repeated only if there was disturbance in the biochemical parameter.

Data availability statement

The data that support the findings of this study are available from the corresponding author upon request.

Discussion

Eight out of 10 patients in our study were of primary hyperparathyroidism. In remaining two patients with CKD it was unclear if these patients had adenomas because of sporadic primary hyperparathyroidism or were they tertiary hyperparathyroidism with asymmetrical hyperplasia, since it is known that 20% of patients with tertiary hyperparathyroidism develop autonomously functioning parathyroid adenomas.[23]

Surgical parathyroidectomy has been the procedure of choice and standard of care for patients with symptomatic parathyroid adenoma.[6] Medical therapy with calcimimetics (like cinacalcet) are considered in select subset of patients, like the patients with hyperplasia in all glands rather than an isolated adenoma, patients with persisting hyperparathyroidism following unsuccessful surgery or patients who are inoperable cases because of comorbidities, and patients who are

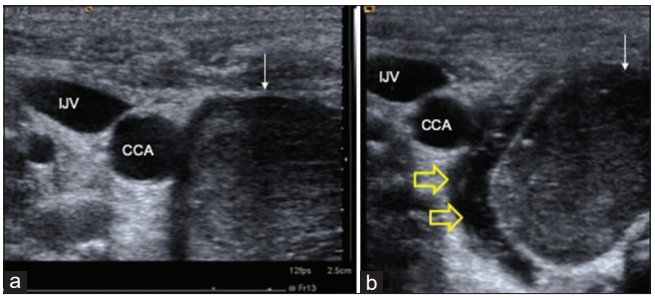

Figure 4: (a) Transverse ultrasound scan of left inferior parathyroid adenoma (arrow) abutting the CCA. (b) layer of hypoechoic fluid along the medial aspect of adenoma (open arrow) created by hydro-dissection. Abbreviation: CCA = Common carotid artery, IJV = Internal Jugular Vein

Table 2: Sizes of parathyroid adenoma

Patient	Size of Nodule (in mm)
1	20 x 19
2	13 x 12
3	14 x12
4	7.5 x 5.3
5	35 x 30
6	9 x 5
7	12 x 5.4
8	12 x 9
9	22 x 21
10	13 x 5

asymptomatic hypercalcaemic and are not candidates for surgery.[24] However, it is expensive and causes dose□dependent gastrointestinal disturbance.[24,25] Thus, long-term use of Cinacalcet is limited by patient compliance and is most often indicated as a temporary therapy until a definitive curative therapy can be carried out.[26] In the current study, surgical consultation was taken for all the 10 patients who were deemed as poor risks for surgery and hence this alternate modality was considered for treatment.

These parathyroid adenomas are diagnosed and localized with Tc 99m Sestamibi scan and USG evaluation with the sensitivity and specificity of 87% and 71%, respectively.[27] In our study group, the decision to ablate the adenomas were taken on a case-to-case basis by a multidisciplinary team. Three of the 10 patients were awaiting liver transplantation and required definitive treatment for hypercalcemia secondary to parathyroid adenoma for clearance for liver transplant surgery. In two patients with CKD, PTH levels were significantly higher than normal in spite of medical management for more than 6 months and both patients had significant symptoms. In two patients of necrotising acute pancreatitis, the parathyroid adenomas were considered as precipitating etiological factors and inspite of ongoing medical management (with Injection Calcitonin) a clinical decision was taken to treat it early. Two patients with CLD were counselled to enrol into the liver transplant program and were hence advised to undergo ablation.

Table 3a: The Pre and Post-ablation serum calcium levels

Serum Calcium Levels (in mmol/L)						
Patients	Pre-ablation	Post-ablation				
		72 hours	1 Month	6 Month	12 Month	18 Month
1	2.92	2.45	-	-	-	-
2	3.14	2.35	2.4	2.45	2.42	2.4
3	2.77	2.54	2.17	2.22	-	-
4	2.99	2.5	2.5	2.47	2.4	2.3
5	2.67	2.45	*	*	*	*
6	2.82	2.5	2.4	2.45	-	-
7	2.67	2.1	2.07	2.02	2.22	-
8	2.67	2.45	2.52	2.45	2.47	2.35
9	2.92	2.45	2.4	2.5	2.42	2.45
10	2.59	2.5	-	-	-	-

- Lost to follow up * Demise at 15th day post ablation

Table 3b: The Pre and Post ablation PTH levels

Parathormone (PTH) Levels (in ng/L)			
Patients	Pre-ablation	Post-ablation	
		7 days	6 months
1	610	24.4	-
2	1131	28	27.8
3	111.1	20.7	22.2
4	181.7	25	29.4
5	10148.5	54.2	*
6	94.5	19.1	15
7	253.9	24	20.6
8	119.7	15	15.9
9	780	34.2	36.6
10	3000	41.7	-

- Lost to follow up * Demise at 15th day post ablation

In recent time percutaneous ablative treatment methods have been used successfully in patients who were either unfit for or refused surgical treatment.[15,26]

Sormaz *et al.*[15] evaluated results of percutaneous USG guided RFA in five hyperparathyroid patients with a single hyperfunctioning parathyroid lesion, who could not undergo or refused surgery because of severe cardiovascular or pulmonary comorbidities. The authors demonstrated the potential feasibility of RFA for hyperparathyroidism specially in patients with small parathyroid lesions. All patients became normo-calcemia on the post-ablation 1st day and continued to remain so at the 6-month follow-up. The post-ablation PTH levels normalized in three patients with small (<30 mm) sized lesion but it remained elevated in two with size ≥30 mm. In a study by Korkusuz H *et al.*,[26] the authors aimed to assess the feasibility of RFA in 9 patients with primary parathyroid adenoma. The procedure resulted in a statistically significant (P = 0.004) decrease of serum PTH levels and also an overall reduction in calcium levels. There were no procedure related complications like infections, persisting pain or nerve injury, thus proving bRFA to be an effective, safe, applicable and well tolerable thermoablative technique in the treatment of parathyroid adenoma. Kim BS *et al.*[17] reported RFA in a young patient with hyperparathyroidism. RFA was done after a saline injection inferomedial to the parathyroid, to prevent burn injury to the recurrent laryngeal nerve. The completeness of tissue ablation was evaluated based on Doppler ultrasound imaging and intact parathyroid hormone (iPTH) level immediately after RFA. There were no peri-procedural complications and the Serum iPTH levels normalized during the 20-month follow-up.

Carrafiello *et al.*[28] performed RFA in a patient with a recurrent secondary hyperparathyroidism with absolute contraindication for surgery. Pre- and post-procedure contrast-enhanced US was used to identifying real time hemodynamic vascular changes and necrotic tissue. Clinical and laboratory follow-up showed a resolution of hyperparathyroidism with normal levels of PTH, serum calcium, and alkaline phosphatase levels 6 months after RFA. Imaging follow-up at 2 weeks and 1, 3, and 6 months after procedure demonstrated complete ablation of parathyroid tissue. These, and few other case reports on ablation of parathyroid adenoma[13,14,18] and large number of published data on ablation of benign thyroid nodules establishing its safety profile[29-32] formed the basis of using Radiofrequency ablation as treatment modality in our patients.

Hence the protocol for ablation used in our study was similar to that used for ablation of benign thyroid nodules.[31] However, larger experience is imperative for optimizing and validating RFA protocols for parathyroid adenoma ablation. We feel that the use of RFA as a minimal invasive treatment for parathyroid adenomas would open a gateway for larger study and could refine the indication for treating parathyroid adenoma by this modality.

Virtual absence of procedure related complications and feasibility of performing the procedure bed-side along with obviating the need for general anesthesia can potentially make it a preferred treatment method for critically ill patients and patients with significant comorbidities. The 30-day mortality

of 10% (1 patient with severe acute necrotising pancreatitis requiring ventilator support, died of multiorgan failure 15 days post-procedure) in the current study highlights the need to define the inclusion criteria for even minimally invasive procedures such as ablation for parathyroid adenomas, especially in critically ill patients. Cosmetic implications of scar formation and higher chances of recurrent laryngeal nerve damage, both associated with surgery, are virtually unknown with radiofrequency ablation and hence make it a viable option for patients not wanting to undergo surgery.

Ethanol ablation has also been tried as a method of treatment for parathyroid adenoma and secondary hyperplasia but is mostly done for lesions which are predominantly cystic. It invariably needs to be repeated as there is a higher incidence of recurrence of hypercalcemia.[13,33-36]

Histopathological confirmation prior to RFA was not carried out in our study. The absence of histopathological confirmation prior to treatment of the adenomas could be termed as a limitation of such an approach. However, the incidence of parathyroid carcinoma which is less than 1% of all the adenomas[37] and solitary hyperplasia which is virtually unknown should be brought into the context when selecting non-surgical treatments for high risk surgical patients.

The changes in biochemical parameters were used for objective evaluation of treatment outcome in the current patient group. Both serum PTH and calcium levels reached to normal range 72 h after ablation. Measurement of biochemical parameters to evaluate technical success have already been emphasized in surgical literature. In the only other case series published in English literature on use of ablation for parathyroid adenoma, reduction of serum calcium levels during the first 4--6 h were reported in only 5.7% of patients, though the reduction was not statistically significant. PTH levels were also reported to become normal in post-ablative period,[26] however no definitive time line has been suggested for ideal time interval for measuring biochemical parameters post-ablation. In recent years, there has been trend toward focused parathyroidectomy as means of minimal invasive surgical treatment for parathyroid adenomas. Focused parathyroidectomy entails an image-guided exploration of a single parathyroid adenoma with the utilization of intraoperative parathyroid hormone (PTH) monitoring to define a biochemical cure. This has been emphasized in a study where importance of intraoperative PTH levels, measured in all patients undergoing focused parathyroidectomy, had drop of greater than 50% from the pre-excision values within 10 min.[38] However on the other hand, another study of 20 patients reported that focused parathyroidectomy utilizing preoperative imaging with no intraoperative PTH monitoring resulted in 95% successful outcome.[39] Hence, basis on these studies one can consider refining the protocol for biochemical monitoring during ablation, immediate post-ablation period and using same day post-procedure PTH levels to evaluate outcomes.

In our study, serum calcium level was evaluated 72 h of the ablation, and not earlier, with the rationale that the remaining at least three parathyroid glands would be maintaining normal calcium levels. Studies on focused parathyroidectomy have used postoperative assessment of serum calcium levels varying from 2 h post operatively[40] to within 24 h[39] for patient monitoring as a determinant of a successful treatment and have not reported hypocalcemia in any of their patients in the initial postoperative period. However, till the experience is more robust it may be prudent to maintain a closer monitoring of serum calcium in the postoperative period. A longer follow-up with clinical and biochemical evaluation is therefore imperative for establishing role of percutaneous radiofrequency ablation as a long-term treatment option for symptomatic hyperparathyroidism because of solitary adenoma. This is especially important because surgical data suggest that recurrence rate of hyperparathyroidism is 14.8% with a third of them diagnosed more than 10 years after surgery.[41]

Ectopic parathyroid adenomas are known to occur in 0.3--8% of cases of primary hyperpararthyroidism[42] and are commonly found in anterior mediastinum (20%), posterior mediastinum (5--10%), thyroid gland (5%), and the carotid sheath (1%).[43] These are often a source of persistent hypercalcemia after parathyroidectomy in approximately 3--5% cases, thus requiring re-interventions.[44,45] Traditionally mediastinal adenomas are surgically excised through sternotomy, lateral thoracotomy, or video-assisted mediastinal/thoracoscopic surgery, which are associated with significant risk of morbidity seen in up to 21% of case.[46] Minimally invasive technique of cryoablation has been described to treat anterior mediastinal ectopic parathyroid adenomas in various case reports and have shown to be safe and effective alternative to surgery or embolization in lesions that are percutaneously accessible.[43,46] There is lack of published literature on use of RFA to treat these ectopic parathyroid adenomas in the mediastinum. In our study we did not encounter any patient with ectopic parathyroid adenoma. However, successful outcomes of cryoablation in such cases may form a basis for attempting RFA to treat any such lesions with a safely accessible percutaneous approach.

Conclusion

This initial experience of RFA for parathyroid adenomas, though in a small group of patients, has proved to be safe and effective treatment method for patients suffering from hyperparathyroidism and hypercalcemia due to parathyroid adenoma. The inherent advantages of this minimally invasive treatment method make a case for a larger study to validate the role of RF as a preferred treatment method in all cases of hyperparathyroidism with a functioning parathyroid adenoma.

Ethics approval

The protocol of this study was approved by the Ethics Committee of the Institutional Review Board.

Consent to participate

Written informed consent was obtained from all patients before they underwent RFA.

Consent for publication

Consent for publication is included in the written informed consent. Patients signed informed consent regarding publishing their data

Availability of data and material

The data that support the findings of this study are available from the corresponding author upon request.

Code availability

Not applicable.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Elfenbein DM, Madkhali T, Alhefdhi A, Chen H, Elfenbein D. Primary hyperparathyroidism Address for Correspondence. Ulus Cerrahi Derg 2016;32:58-66.
2. Sivula A, Ronni-Sivula H. The changing picture of primary hyperparathyroidism in the years 1956-1979. Ann Chir Gynaecol 1984;73:319-24.
3. Jorde R, Bønaa KH, Sundsfjord J. Primary hyperparathyroidism detected in a health screening. The Trømsø study. J Clin Epidemiol 2000;53:1164-9.
4. Wermers RA, Khosla S, Atkinson EJ, Achenbach SJ, Oberg AL, Grant CS, *et al*. Incidence of primary hyperparathyroidism in Rochester, Minnesota, 1993-2001: An update on the changing epidemiology of the disease. J Bone Min Res 2006;21:171-7.
5. AACE/AAES Task Force on Primary Hyperparathyroidism. The American Association of Clinical Endocrinologists and the American Association of endocrine surgeons position statement on the diagnosis and management of primary hyperparathyroidism. Endocr Pract 2005;11:49-54.
6. Bilezikian JP, Brandi ML, Eastell R, Silverberg SJ, Udelsman R, Marcocci C, *et al*. Guidelines for the management of asymptomatic primary hyperparathyroidism: Summary statement from the fourth international workshop. J Clin Endocrinol Metab 2014;99:3561-9.
7. Allendorf J, DiGorgi M, Spanknebel K, Inabnet W, Chabot J, Logerfo P. 1112 Consecutive bilateral neck explorations for primary hyperparathyroidism. World J Surg. World J Surg 2007;31:2075-80.
8. Cohen MS, Finkelstein SE, Brunt LM, Haberfeld E, Kangrga I, Moley JF, *et al*. Outpatient minimally invasive parathyroidectomy using local/regional anesthesia: A safe and effective operative approach for selected patients. Surgery 2005;138:681-9.
9. Black MJ, Ruscher AE, Lederman J, Chen H. Local/cervical block anesthesia versus general anesthesia for minimally invasive parathyroidectomy: What are the advantages? Ann Surg Oncol 2007;14:744-9.
10. Rajeev P, Stechman MJ, Kirk H, Gleeson F V, Mihai R, Sadler GP. Safety and efficacy of minimally-invasive parathyroidectomy (MIP) under local anaesthesia without intra-operative PTH measurement. Int J Surg. Int J Surg 2013;11:275-7.
11. Chau JKM, Hoy M, Tsui B, Harris JR. Minimally invasive parathyroidectomy under local anesthesia: Patient satisfaction and overall outcome. J Otolaryngol Head Neck Surg 2010;39:361-9.
12. Sen S, Cherian AJ, Ramakant P, Reka K, Paul MJ, Abraham DT. Focused parathyroidectomy under local anesthesia-A feasibility study. Indian J Endocrinol Metab 2019;23:67-71.
13. Shenoy MT, Menon AS, Nazar PK, Moorthy S, Kumar H, Nair V, *et al*. Radiofrequency ablation followed by percutaneous ethanol ablation leading to long-term remission of hyperparathyroidism. J Endocr Soc 2017;1:676-80.
14. Alherabi AZ, Marglani OA, Alfiky MG, Raslan MM, Al-Shehri B. Percutaneous ultrasound-guided alcohol ablation of solitary parathyroid adenoma in a patient with primary hyperparathyroidism. Am J Otolaryngol 2015;36:701-3.
15. Sormaz IC, Poyanlı A, Açar S, İşcan AY, Ozgur İ, Tunca F, *et al*. The results of ultrasonography-guided percutaneous radiofrequency ablation in hyperparathyroid patients in whom surgery is not feasible. Cardiovasc Intervent Radiol 2017;40:596-602.
16. Jeong WK, Baek JH, Rhim H, Kim YS, Kwak MS, Jeong HJ, *et al*. Radiofrequency ablation of benign thyroid nodules: Safety and imaging follow-up in 236 patients. Eur Radiol 2008;18:1244-50.
17. Kim BS, Eom TI, Kang KH, Park SJ. Radiofrequency ablation of parathyroid adenoma in primary hyperparathyroidism. J Med Ultrason 2014;41:239-43.
18. Xu SY, Wang Y, Xie Q, Wu HY. Percutaneous sonography-guided radiofrequency ablation in the management of parathyroid adenoma. Singapore Med J 2013;54:e137-40.
19. Kim JH, Baek JH, Lim HK, Ahn HS, Baek SM, Choi YJ, *et al*. 2017 Thyroid radiofrequency ablation guideline: Korean society of thyroid radiology. Korean J Radiol 2018;19:632-55.
20. Papini E, Monpeyssen H, Frasoldati A, Hegedüs L. 2020 European thyroid association clinical practice guideline for the use of image-guided ablation in benign thyroid nodules. Eur Thyroid J 2020;9:172-85.
21. Papini E, Pacella CM, Solbiati LA, Achille G, Barbaro D, Bernardi S, *et al*. Minimally-invasive treatments for benign thyroid nodules: A Delphi-based consensus statement from the Italian minimally-invasive treatments of the thyroid (MITT) group. Int J Hyperthermia 2019;36:376-82.
22. Baek JH, Lee JH, Valcavi R, Pacella CM, Rhim H, Na DG. Thermal ablation for benign thyroid nodules: Radiofrequency and laser. Korean J Radiol 2011;12:525-40.
23. Pitt SC, Sippel RS, Chen H. Secondary and tertiary hyperparathyroidism, state of the art surgical management. Surg Clin North Am 2009;89:1227-39.
24. Rothe HM, Liangos O, Biggar P, Petermann A, Ketteler M. Cinacalcet treatment of primary hyperparathyroidism. Int J Endocrinol 2011;2011:415719. doi: 10.1155/2011/415719.
25. Grey A. Nonsurgical management of mild primary hyperparathyroidism - A reasonable option. Clin Endocrinol (Oxf) 2012;77:639-44.
26. Korkusuz H, Wolf T, Grünwald F. Feasibility of bipolar radiofrequency ablation in patients with parathyroid adenoma: A first evaluation. Int J Hyperthermia 2018;34:639-43.
27. Tawfik AI, Kamr WH, Mahmoud W, Abo Shady IA, Mohamed MH. Added value of ultrasonography and Tc-99m MIBI SPECT/CT combined protocol in preoperative evaluation of parathyroid adenoma. Eur J Radiol Open 2019;6:336-42.
28. Carrafiello G, Laganà D, Mangini M, Dionigi G, Rovera F, Carcano G, *et al*. Treatment of secondary hyperparathyroidism with ultrasonographically guided percutaneous radiofrequency thermoablation. Surg Laparosc Endosc Percutan Tech 2006;16:112-6.
29. Mauri G, Sconfienza LM. Percutaneous ablation holds the potential to substitute for surgery as first choice treatment for symptomatic benign thyroid nodules. Int J Hyperthermia 2017;33:301-2.
30. Gharib H, Papini E, Garber JR, Duick DS, Harrell RM, Hegedüs L, *et al*. American association of Clinical Endocrinologists, American college of endocrinology, and Associazione Medici Endocrinologi medical guidelines for clinical practice for the diagnosis and management of thyroid nodules-2016 update. Endocr Pract 2016;22:622-39.
31. Baek JH, Kim YS, Lee D, Huh JY, Lee JH. Benign predominantly solid thyroid nodules: Prospective study of efficacy of sonographically guided radiofrequency ablation versus control condition. Am J Roentgenol 2010;194:1137-42.
32. Deandrea M, Sung JY, Limone P, Mormile A, Garino F, Ragazzoni F, *et al*. Efficacy and safety of radiofrequency ablation versus observation for nonfunctioning benign thyroid nodules: A randomized controlled international collaborative trial. Thyroid 2015;25:890-6.
33. Schamp S, Dünser E, Schuster H, Kramer-Deimer J, Kettenbach J, Funovics M, *et al*. Ultrasound-guided percutaneous ethanol ablation of parathyroid hyperplasia: Preliminary experience in patients on chronic dialysis. Ultraschall Med 2004;25:131-6.

34. Veldman MW, Reading CC, Farrell MA, Mullan BP, Wermers RA, Grant CS, *et al*. Percutaneous parathyroid ethanol ablation in patients with multiple endocrine neoplasia type 1. Am J Roentgenol 2008;191:1740-4.
35. Sung JY, Baek JH, Kim KS, Lee D, Ha EJ, Lee JH. Symptomatic nonfunctioning parathyroid cysts: Role of simple aspiration and ethanol ablation. Eur J Radiol. Eur J Radiol 2013;82:316-20.
36. Singh Ospina N, Thompson GB, Lee RA, Reading CC, Young WF. Safety and efficacy of percutaneous parathyroid ethanol ablation in patients with recurrent primary hyperparathyroidism and multiple endocrine neoplasia type 1. J Clin Endocrinol Metab 2015;100:E87-90.
37. Marcocci C, Cetani F, Rubin MR, Silverberg SJ, Pinchera A, Bilezikian JP. Parathyroid carcinoma. J Bone Miner Res 2008;23:1869-80.
38. Pradhan R, Gupta S, Agarwal A. Focused parathyroidectomy using accurate preoperative imaging and intraoperative PTH: Tertiary care experience. Indian J Endocrinol Metab 2019;23:347-52.
39. Abdelfatah El-hady H, Saleh Radwan H. Focused parathyroidectomy for single parathyroid adenoma: A clinical account of 20 patients. Electron Physician 2018;10:6974-80.
40. Kim WW, Rhee Y, Ban EJ, Lee CR, Kang SW, Jeong JJ, *et al*. Is focused parathyroidectomy appropriate for patients with primary hyperparathyroidism? Ann Surg Treat Res 2016;91:97-103.
41. Lou I, Balentine C, Clarkson S, Schneider DF, Sippel RS, Chen H. How long should we follow patients after apparently curative parathyroidectomy? Surg 2017;161:54-61.
42. Alam N, Adimoolam K, Gougler P, Okwuwa I and Li W. Primary Hyperparathyroidism from an Ectopic Retrosternal Parathyroid Adenoma. Austin J Clin Case Rep. 2015;2:1068.
43. Meek J, Fletcher S, Kessler M, Komarraju A, Privat C, Meek M. Percutaneous transsternal cryoablation of ectopic parathyroid adenoma in the anterior mediastinum. J Endocr Soc 2017;1:1287-92.
44. Udelsman R. Six hundred fifty-six consecutive explorations for primary hyperparathyroidism. Ann Surg 2002;235:665-72.
45. Zarebczan B, Chen H. Influence of surgical volume on operative failures for hyperparathyroidism. Adv Surg 2011;45:237-48.
46. Smirniotopoulos J, Pua BB, Abbey-Mensah G, Zarnegar R, Barclay J, Winokur RS. CT–Guided cryoablation of a substernal mediastinal ectopic parathyroid adenoma. J Vasc Interv Radiol 2017;28:614-6.