



A Single Center Retrospective Analysis of Patients With Recurrent Papillary Thyroid Carcinoma Undergoing Radiofrequency Ablation

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ABSTRACT

Background Radiofrequency ablation (RFA) is used in selected patients with recurrent or metastatic thyroid cancer who have high surgical risk or do not accept surgical treatment. However, long-term follow-up data are limited. Here, we present our single-center experience with the use of RFA in the treatment of recurrent or metastatic papillary thyroid carcinoma (PTC).

Material and Methods Patients who underwent RFA for recurrent or metastatic PTC at Bursa Uludag University Faculty of Medicine between September 2014 and January 2021 were included. The data in the endocrinology outpatient clinic follow-ups of the patients were analyzed retrospectively.

Results A total of 10 patients, 11 RFA procedures, and 13 residual or metastatic sites were evaluated. The mean age was 44.50±14.04 years. The mean largest diameter of the tumor in which RFA was applied was 11.85±5.95 mm. Patients developed no major complications. Two patients experienced minor complications. The mean follow-up duration was of 51.20±19.86 months. During the follow-up period, 12 (92.30%) of 13 RFA sites completely disappeared. In one patient (7.69%) residual tumor tissue was detected after RFA. There was no recurrence at the procedure site. A significant decrease was found in the largest diameter of the treated regions after RFA (p=0.002). Thyroglobulin and anti-thyroglobulin levels were not significantly different before and after RFA (p=0.44 and p=1.00, respectively).

Conclusions RFA is highly effective and safe for locally recurrent PTC. It shows promise as an alternative to surgery to control locoregional recurrence of PTC.

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Introduction

Thyroid cancer is the most common endocrinological malignancy, ranking in ninth place among all cancers worldwide. It has been reported that 5-year relative survival of thyroid cancer in Europe is around 80-90%.¹ The incidence of differentiated thyroid cancers has been increasing in recent years.^{2,3} The most common subtype of thyroid cancer is papillary thyroid carcinoma (PTC). Most patients can be successfully treated with initial surgery and, if necessary, radioactive iodine therapy. However, local recurrence or distant metastasis occurs in the follow-up of some patients. Recurrent disease in operated patients mostly detected in the surgical bed or lymph nodes in the neck.⁴ When recurrent thyroid cancers are detected, the standard treatment is reoperation followed by radioactive iodine therapy.^{5,6} However, repeated neck operations present a higher risk of complications and can negatively affect the patient's quality of life.^{6,7} In addition, some patients may be at high risk for surgery due to comorbidities. So, there is a need for alternative treatment options in recurrent or metastatic thyroid cancer.

Radiofrequency ablation (RFA) is a minimally invasive technique that provides coagulation necrosis in tissue. It has been used in the treatment of various solid tumors. In thyroid disease, RFA particularly has been tried in benign thyroid nodules.⁵ However, there have not been enough studies on its use in thyroid cancer, and long-term follow-up data are limited.^{5,8,9} RFA is mostly applied in selected patients with recurrent or metastatic thyroid cancer who have high surgical risk or do not accept surgical treatment.^{8,10} Here, we present our single-center experience with the use of RFA in the treatment of recurrent or metastatic PTC. The aim of this retrospective analysis is to evaluate the efficacy and safety of RFA at long-term follow-up.

Material and Methods

Patients

A Patients who underwent RFA for metastatic or recurrent PTC at Bursa Uludag University Faculty of Medicine between September 2014 and January 2021 were included in the study. The exclusion criterias were age <18 years, follow-up period of <12 months, incomplete follow-up data. Finally, we enrolled 10 patients, 11 RFA procedures, and 13 residual/metastatic sites (nine metastatic neck lymph nodes, four thyroid lodges) in this retrospective analysis. Recurrence or lymph node metastasis was confirmed by ultrasonography (US)-guided fine-needle aspiration biopsy in all patients. The data in the endocrinology outpatient clinic follow-ups of the patients were analyzed retrospectively.

The data collected included age, gender, type and number of surgery, radioactive iodine therapy, presence of distant metastases before and after RFA, the time between diagnosis and RFA, RFA location and size, anesthesia, complications, follow-up time after RFA, sonographic and other imaging modalities (if available) findings, histopathological findings, recurrence in RFA region, thyroglobulin and anti-thyroglobulin levels (before and after RFA, and the last measured).

This study was approved by our institutional review board.

Ablation Procedures

All US-guided RFA procedures were performed by experienced radiologists in our center. A radiofrequency generator (STARmed) and a 17- or 18-gauge internally cooled electrode with 5-, 7- or 10-mm active tips were used based on the volume of the target tumor. The RFA power was 15-60 W. RFA procedure was performed using the moving-shot and hydrodissection technique. The ablation procedure was terminated when the tumor was entirely covered with hyperechoic zone.

Statistical Analysis

Analysis of the data was performed with SPSS (version 22.0) statistical software. Continuous data were presented as mean±SD (range). The changes in serum thyroglobulin and anti-thyroglobulin levels and the largest diameter of the lesions before and after RFA were compared using Wilcoxon signed-rank tests. A p value <0.05 was considered as statistically significant.

Results

Although twelve patients underwent RFA for the treatment of metastatic or recurrent PTC in our hospital between September 2014 and January 2021, two patients were excluded from the study due to insufficient follow-up data. Ten patients with thyroid papillary carcinoma (eight females, two males) were included in the study. The main clinical features of patients before RFA are summarized in Table 1. A total of 11 RFA procedures and 13 residual/metastatic sites (nine neck lymph nodes, one isthmus, one right thyroid lobe, two left thyroid lobes) were evaluated. The mean age of the patients was 44.50 ± 14.04 years (age range: 24-63). One patient underwent 2 RFA procedures from different regions (right zone 5 and right zone 2A, respectively). All patients had undergone surgery before RFA. The mean number of surgeries before RFA was 2 (range 1-3). Total thyroidectomy was performed in 5 patients, right lobectomy in 1 patient, total thyroidectomy and neck lymph node dissection in 3 patients, and pulmonary wedge resection in addition to total thyroidectomy and neck lymph node dissection in 1 patient. All patients received radioactive

iodine therapy. Two patients (20%) had distant metastases before RFA (one mediastinal lymph node, one lung).

The mean time between the diagnosis of papillary carcinoma and the RFA procedure was 58.82 ± 53.34 (range 7-156) months. Of the 11 RFA procedures, one was performed under general anesthesia and ten under local anesthesia. In two of the RFA procedures, ablation was applied to two regions simultaneously. The mean largest diameter of the lesion in which RFA applied was 11.85 ± 5.95 mm (range 7-30 mm).

There were no patients who developed serious complications after RFA. Minor complications occurred in two patients (18.18%). One patient had swelling in the neck lasting for one week, and one patient had mild hoarseness lasting two weeks. No delayed complication was found during the follow-up period. The mean follow-up data of 51.20 ± 19.86 (range 26-88) months after RFA were analyzed (Table 2). After the RFA procedure, all patients had US evaluation, thyroglobulin, and anti-thyroglobulin results. In the follow-up of the patients, 12 (92.30%) of 13 sites where RFA was applied, completely disappeared. Residual tumor tissue was detected in one patient (7.69%)

Table 1. Baseline patient characteristics before radiofrequency ablation.

Patient No.	Sex/age (years)	Type of surgery	Distant metastasis	Radiofrequency ablation location/level	Size (mm)
1	F/63	Total thyroidectomy	No	Left III Isthmus	7x7 30x30
2	F/46	Total thyroidectomy	No	Left VI	9x8
3	F/61	Total thyroidectomy	Mediastinal lymph node	Left thyroid bed	12x12
4	F/61	Total thyroidectomy	No	Right thyroid bed	15x10
5	F/43	Total thyroidectomy, neck dissection pulmonary wedge resection	Lung	Right IB Right IIB	10x10 10x10
6	M/47	Total thyroidectomy, neck dissection	No	Right V Right IIA	10x5 14x12
7	F/26	Total thyroidectomy, neck dissection	No	Left IIA	11x5
8	F/38	Right lobectomy	No	Right II-V junction	7x7
9	M/36	Total thyroidectomy	No	Right IB-III junction	11x10
10	F/24	Total thyroidectomy, neck dissection	No	Left thyroid bed	8x5

three months after RFA. It was in the left thyroid lodge and had a large diameter of 15 mm. This patient was treated with surgery and radioactive iodine therapy. No recurrence was observed at the procedure site in any of the patients who underwent RFA. A significant decrease was found in the largest diameter of the 13 treated regions after RFA compared to the pre-procedure ($p=0.002$). The mean serum thyroglobulin before RFA was 5.49 ± 12.87 (range 0.2-43.8) mcg/L and after RFA 4.91 ± 13.44 (range 0.14-45.3) mcg/L. There was no significant difference between the thyroglobulin levels before and after RFA ($p=0.44$). The mean final thyroglobulin level in the follow-ups of the patients was 7.46 ± 16.16 (range 0.14-48.67). There was no significant difference between pre-RFA and the last thyroglobulin levels ($p=0.07$). No significant difference was found between the anti-thyroglobulin levels (IU/ml) of the patients before and after RFA ($p=1.00$). When the anti-thyroglobulin levels before RFA and the last measured anti-thyroglobulin levels were compared, no statistically significant difference

was found ($p=0.85$). In the follow-up of four patients, metastases were detected outside the area where RFA was applied. All patients were alive at the time of study conducted.

Discussion

This single-center study showed the long-term effectiveness of RFA for controlling locally recurrent PTC. The complete disappearance rate after RFA was high (92.30%), and no recurrence was observed at the procedure site during long-term follow-up. However, there was no decrease in thyroglobulin and anti-thyroglobulin levels after RFA. Additionally, metastasis outside of the RFA area was detected in four patients. These results are consistent with the knowledge that RFA is only effective in locoregional control. Regarding complications, the safety of the RFA procedure was demonstrated. Minor complications occurred in two of 11 procedures in the study. None of the patients experienced any life-threatening or delayed complications.

Table 2. Long-term follow-up results of patients after radiofrequency ablation.

Patient No.	Follow-up time (month)	Complications after RFA	Residual tumor in RFA region	Tg (mcg/L)			Anti-Tg (IU/mL)		Metastasis after RFA
				Before RFA	After RFA	At last follow-up	Before RFA	After RFA	
1	88	No	No	0.20	0.56	48.67	148.1	145.9	Neck 2B, neck 5 sternoclavicular joint, lung
2	76	No	No	5.69	0.57	1.22	1.00	0.70	No
3	63	No	Left thyroid bed	43.8	45.3	29.20	0.80	3.40	Supraclavicular
4	51	Mild hoarseness	No	0.20	0.20	0.20	0.60	0.50	No
5	50	No	No	0.43	0.30	0.14	256.4	572.1	Lung, bone
6	47	Swelling in the neck	No	5.69	3.69	1.76	1.20	1.30	Neck 2A
7	46	No	No	0.47	0.20	0.14	24.2	5.30	No
8	38	No	No	1.31	0.30	0.17	2.20	1.00	No
9	27	No	No	0.20	0.14	0.14	9.90	12.7	No
10	26	No	No	0.30	0.30	0.22	1.00	1.30	No

RFA: radiofrequency ablation, Tg: thyroglobulin.

Surgery, followed by radioactive iodine therapy, is the established therapeutic approach for neck recurrences of PTC. Revision surgery for the recurrent disease has some challenges due to fibrosis caused by scar tissue formation and distortion of tissue planes. Thus, identification and preservation of the recurrent laryngeal nerve and parathyroid glands become difficult.^{5,6,11} Furthermore, detecting small recurrent lesions may be difficult without US guidance.¹²

Recently, thermal ablative techniques (RFA, laser ablation, microwave ablation) and chemical ablative approaches (ethanol ablation) have been reported as an alternative to surgery for selected patients. Shin JE et al. compared RFA and ethanol ablation for the treatment of recurrent thyroid cancer. They found that the effectiveness of RFA was slightly higher. However, RFA was associated with higher voice complications.⁹ There have been some reports regarding RFA for the treatment of thyroid carcinoma.^{4,5,8-18} However, these studies have some limitations such as a small number of patients and short-term (mostly <5 years) follow-up duration.¹¹ Our study has a relatively long follow-up period compared to other reports. In recent years, Chung SR et al.¹² have reported longer-term outcome data of radiofrequency ablation for locally recurrent PTC. The mean follow-up duration was 80±17.3 months. Twenty-nine patients were reviewed and a mean tumor volume reduction of 99.5±2.9% was obtained. There were no delayed complications associated with RFA. In our study, although the volume could not be calculated due to insufficient size data, we showed a significant decrease in the largest diameter of tumor. Kim JH et al.¹³ evaluated 73 patients with recurrent thyroid cancer. They demonstrated a high complete disappearance rate of 86.1% and low recurrence rate of 11.5% after three years of follow-up. They reported only one complication, transient vocal cord paralysis. A meta-analysis including 189 patients (mean six months of follow-up) demonstrated a significant decrease of tumor volume, the largest diameter of tumor, and thyroglobulin level after RFA. For malignant nodules, the overall complication rate was 10.98%, which is comparable with our results.¹⁷ In our study, we also evaluated anti-thyroglobulin levels which may be associated with tumor burden.¹⁹ We

found a decrease in neither thyroglobulin nor anti-thyroglobulin levels with the treatment of RFA. It may be due to the small patient population or the presence of distant metastasis before RFA.

American Thyroid Association (ATA) suggests RFA in high-risk surgical patients or patients refusing additional surgery.²⁰ A recently published review article suggested RFA treatment for the early localized disease in patients who are poor operative candidates or have other reasons to avoid surgery.⁵

Limitations

Limitations of our study include the small number of patients and retrospective design. Further long-term follow-up or controlled prospective trials are needed.

Conclusions

RFA is highly effective and safe, when performed in experienced centers, for locally recurrent PTC and might be a promising treatment option to control locoregional recurrence of PTC.

Acknowledgment

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Conflict of interest

The authors declared that there are no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Authors' Contribution

Study Conception: CA, EA; Study Design: EA; Supervision: CE, SC, OOG; Data Collection and/or Processing: EH, CA, FMS; Statistical Analysis and/or Data Interpretation: EA; Literature Review: EH, EA; Manuscript Preparation: EH; and Critical Review: CE, EE, FMS.

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