

# VIETNAMESE EXPERT CONSENSUS ON RADIOFREQUENCY ABLATION (RFA) FOR THYROID NODULES (2025)

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## Abbreviations

RFA	:	Radiofrequency ablation
FNA	:	Fine-needle aspiration
CNB	:	Core-needle biopsy
TSH	:	Thyroid-stimulating hormone
FT4	:	Free thyroxine
VRR	:	Volume reduction ratio
anti-Tg	:	Anti-thyroglobulin antibody
anti-TPO	:	Anti-thyroid peroxidase antibody
AFTN	:	Autonomously functioning thyroid nodule
RAI	:	Radioactive iodine therapy
PTC	:	Papillary thyroid carcinoma
RTC	:	Recurrent thyroid carcinoma

## Introduction

Radiofrequency ablation (RFA) was first applied to the treatment of thyroid nodules in the early 2000s in South Korea and has since become one of the most important minimally invasive interventional therapies for various types of thyroid nodules. In benign thyroid nodules, RFA reduces nodule volume and improves compressive symptoms and cosmetic concerns, serving as an effective alternative to surgery, particularly in patients who are unwilling or unsuitable for surgical treatment.

In autonomously functioning thyroid nodules, RFA can control excessive hormone secretion, improve clinical symptoms and quality of life, and avoid permanent hypothyroidism, which may occur after surgery or radioactive iodine (I-131) therapy. In papillary thyroid

microcarcinoma, RFA has increasingly been recognized as a curative treatment option for patients who are not suitable candidates for surgery or who refuse surgical intervention, providing high local control rates with a low complication profile. In addition, RFA has demonstrated effectiveness in the treatment of locally recurrent thyroid cancer or metastatic cervical lymph nodes after surgery, serving as an alternative to repeat surgery, which is associated with higher risks due to postoperative adhesion and altered anatomy.

Although numerous recommendations and practice guidelines for thyroid RFA have been published worldwide, substantial differences remain among European, American, and Asian practice patterns. In Vietnam, the clinical application of RFA for thyroid

nodules has expanded rapidly in recent years; however, challenges persist regarding standardization of indications, procedural protocols, and long-term outcome assessment.

## Methods

The Vietnamese Society of Radiology and Nuclear Medicine (VSRNM) and the Vietnamese Society of Interventional Radiology (VSIR) organized an expert workshop on the application of RFA for the treatment of thyroid nodules and adopted a modified Delphi method to develop the “2025 Expert Consensus on the Management of Thyroid Nodules Using Radiofrequency Ablation (RFA).”

The modified Delphi method was applied to assess expert agreement regarding the recommendations. Specifically, it was used to determine consensus on the benefits (clinically meaningful therapeutic benefit) and harms (harms outweighing benefits) of RFA for patients with thyroid nodules.

### Expert Panel

The expert panel consisted of specialists in the following fields: interventional radiology, endocrinology, thyroid surgery, oncology, nuclear medicine, and pathology.

### Consensus Process

The consensus development process included the following steps:

- (1) The steering committee reviewed international studies and treatment guidelines to formulate preliminary RFA recommendations adapted to the Vietnamese clinical setting. An electronic survey was distributed to all panel members, who completed their responses independently and anonymously, without access to the responses of other members.
  - Responses were analyzed using a 9-point Likert scale, ranging from 1 (strongly disagree) to 9 (strongly agree).
  - Consensus was defined as a mean score  $\geq 7.0$  with 0–2 dissenting responses, or a mean score  $\geq 7.0$  with up to three neutral responses (score = 5).
  - A dissenting response was defined as any rating differing from the mean by at least 2 Likert points.
  - If the level of agreement (scores 7–9) was below 67%, the wording of the recommendation was revised based on initial feedback, and a second survey round was conducted.

- (2) During the consensus workshop, each recommendation was presented and discussed with expert panel members and attending physicians, leading to final agreement.

- (3) The final consensus on all recommendations was approved and prepared for publication in a scientific journal.

### Definition of Strength of Recommendation

- Strong recommendation: Applicable to most or nearly all patients in most clinical situations. The benefits of the intervention clearly outweigh the risks, or vice versa.
- Weak recommendation: Applicability may vary depending on clinical circumstances or patient values. The benefits are closely balanced with potential harms and burdens.

Factors considered in grading the strength of recommendations included the quality of evidence, clinical benefits and harms, costs, patient preferences, and values.

## PART 1: RADIOFREQUENCY ABLATION (RFA) FOR BENIGN THYROID NODULES

### Recommendation 1.1 (Strong recommendation)

Radiofrequency ablation (RFA) is indicated for patients with benign thyroid nodules that are large, progressively growing, cause cosmetic concerns, or produce compressive neck symptoms. (1)

1. Large or progressively growing benign thyroid nodules: (3,4)
  - Nodules with a maximum diameter greater than 3 cm.
  - Nodules with a maximum diameter greater than 2 cm that continue to increase in size during follow-up, confirmed on at least two examinations performed at intervals of 3–6 months.

Nodule growth is defined as

1. Increase in size  $\geq 20\%$ : an increase of  $\geq 20\%$  in the maximum diameter compared with the previous measurement.
2. Increase in volume: nodule volume is calculated using three orthogonal diameters-anteroposterior (A), transverse (B), and craniocaudal (C)-according to the formula:

Volume increase is defined as a  $\geq 50\%$  increase compared with the previous measurement or an absolute volume increase of  $\geq 1.0$  mL

## 2. Benign thyroid nodules causing cosmetic concerns:

- Symptom scores may be self-assessed by patients using a 10-cm visual analog scale (VAS; 0–10). (5–7)
- Cosmetic scores may be assessed by physicians as follows:
  - 1 = no palpable mass;
  - 2 = palpable mass without cosmetic concern;
  - 3 = cosmetic concern only during swallowing;
  - 4 = readily visible cosmetic deformity. (5,6,8)
- The need for treatment depends on individual symptoms and cosmetic concerns, which vary according to neck circumference and nodule location. (1,10) Patients with smaller neck circumferences tend to report cosmetic concerns earlier than those with thicker necks. In addition, isthmic nodules may cause cosmetic problems even when smaller than 2 cm.

## 3. Benign thyroid nodules causing compressive neck symptoms:

Compressive symptoms include pain, dysphagia, foreign body sensation, discomfort, neck swelling, and cough. Nodule size or thyroid lobe volume appears to correlate directly with compressive symptoms. (9,10) Most patients with compressive symptoms experience symptom improvement after surgical removal of the nodule and/or thyroid gland. (10) Therefore, nodules with a maximum diameter greater than 2 cm that continue to grow during follow-up may be considered for thyroid RFA based on symptom severity.

*In cases of multinodular goiter with compressive symptoms, RFA does not replace surgery because of limited efficacy and the need for multiple treatment sessions. RFA should be considered only as a palliative treatment targeting the dominant symptomatic nodule in patients who are not surgical candidates.*

*Benign thyroid nodules with extensive coarse calcifications require careful consideration because RFA may be technically challenging and less effective.*

### **Recommendation 1.2 (Strong recommendation)**

Pre-procedural evaluation for RFA of benign thyroid nodules should include:

- (i) confirmation of benignity by at least two ultrasound-guided fine-needle aspirations (FNA) or core-needle biopsies (CNB);
  - (ii) assessment of nodule size, volume, cosmetic score, and symptom score;
  - (iii) evaluation of intranodular vascularity;
  - (iv) thyroid function testing (serum TSH and free thyroxine [FT4]); and
  - (v) informed consent obtained prior to the procedure.
- (i) Cytologic or histologic confirmation

The risk of malignancy in thyroid nodules can be stratified using ultrasound features according to TIRADS systems (K-TIRADS 2021 or ACR-TIRADS 2017). Current guidelines recommend cytologic or histologic confirmation of benignity by FNA or CNB prior to RFA. (4,8,11) The false-negative rate of benign cytology on FNA or benign histology on CNB is low ( $<3\%$ ). (12,13)

A single benign FNA or CNB result is sufficient for nodules classified as TIRADS 2 or TIRADS 3. However, several studies have reported higher false-negative rates for benign FNA results in large nodules ( $>3\text{--}4$  cm). (14–16) Consequently, concern remains regarding false-negative results based on a single benign cytology in large nodules. (20–22) In contrast, the malignancy risk after two benign cytologic results is extremely low (virtually zero) and such nodules can be regarded as benign. (17,18)

FNA or CNB should be performed under ultrasound guidance by physicians with formal training and experience in thyroid ultrasound and TIRADS assessment.

### (ii) Ultrasound assessment

Nodule size, echogenicity, solid component ratio, and intranodular vascularity should be carefully evaluated. Three orthogonal diameters—anteroposterior (A), transverse (B), and craniocaudal (C)—are used to calculate nodule volume using the formula:  $V = A \times B \times C \times \pi / 6$ . (5,19)

Intranodular vascularity is graded according to Adler's classification:

- Grade 0: no vascular signal
- Grade 1: peripheral vascularity only
- Grade 2: moderate vascularity (peripheral and central)
- Grade 3: marked vascularity (diffuse)

### (iv) Laboratory evaluation

Routine laboratory tests include complete blood count, coagulation tests (prothrombin time and activated partial thromboplastin time), and thyroid function tests (TSH and FT4). (5,20)

When serum TSH levels are elevated (>10 mIU/L) with low FT4, endocrinologists should consider thyroid hormone replacement before RFA to optimize recovery. When serum TSH levels are suppressed, endocrinologists should evaluate whether the patient is receiving thyroid hormone therapy or has hyperthyroidism, and euthyroid status should be achieved 4–8 weeks before RFA.

In patients with abnormal platelet counts or coagulation profiles, consultation with a hematologist or cardiologist is recommended to assess antiplatelet or anticoagulant use or underlying bleeding disorders. Anticoagulant therapy should be discontinued before RFA: 7–10 days for aspirin or clopidogrel, 3–5 days for warfarin, and 4–6 hours for heparin. Anticoagulation may be resumed after RFA according to established protocols. (21,27)

Computed tomography (CT) or magnetic resonance imaging (MRI) may be useful for evaluating the substernal extension of benign thyroid nodules. (1)

(v) Informed consent checklist

Patients should be informed that:

1. Treated nodules gradually decrease in size over months to years, with an average volume reduction of approximately 80% at 1 year (range, 64.9–93.9%).
2. The expected number of treatment sessions depends on nodule size and location.
3. Nodule regrowth may occur, particularly in nodules with high intranodular vascularity or those located near critical structures where partial tissue preservation is required.
4. Patients may experience varying degrees of pain during the procedure, usually mild to moderate.
5. Potential complications include bleeding and nerve injury.
6. Patients should inform physicians of any history of thyroid surgery and current medications, including antiplatelet agents, anticoagulants, or thyroid hormone therapy.
7. Post-procedural observation or hospitalization may be required depending on patient condition.

### **Recommendation 1.3 (Strong recommendation)**

Appropriate techniques for RFA of benign thyroid nodules include:

- (i) perithyroidal local anesthesia with lidocaine;
- (ii) hydro dissection;
- (iii) the trans isthmic approach;
- (iv) the moving-shot or fixed-electrode technique;
- (v) appropriate electrode selection;
- (vi) energy control; and
- (vii) continuous real-time ultrasound monitoring.

### **Recommendation 1.4 (Strong recommendation)**

Post-procedural evaluation after RFA should include:

- (i) nodule size, volume, cosmetic score, and symptom score;
- (ii) intranodular vascularity; and
- (iii) thyroid function tests (TSH and FT4).

The volume reduction ratio (VRR) is calculated as:

Treatment success is defined as a volume reduction greater than 50%, decreased intranodular vascularity, marked hypo echogenicity on follow-up ultrasound, and improvement in compressive or cosmetic symptoms.

Residual vascularized tissue on grayscale or color Doppler ultrasound is associated with an increased risk of regrowth. Contrast-enhanced ultrasound may be useful for detecting incompletely ablated areas. (30–33)

Hypothyroidism after RFA of benign thyroid nodules is rare and is most likely related to pre-existing autoimmune thyroid disease. Routine measurement of thyroid autoantibodies before RFA remains controversial when baseline thyroid ultrasound findings are normal. (34–36)

### **Recommendation 1.5 (Strong recommendation)**

RFA is effective in reducing the volume of benign thyroid nodules, improving compressive symptoms, and alleviating cosmetic concerns. Reported volume reduction rates range from 30–50% at 1 month, 50–70% at 6 months, 70–90% at 12–24 months, and remain stable at 80–90% during long-term follow-up (2–10 years). Higher volume reduction rates are observed in smaller nodules ( $\leq 10$ –12 mL).

1. Overall efficacy and volume reduction ratio (VRR)

Meta-analyses have demonstrated substantial volume reduction following RFA, with mean VRRs of 46–78% at

1 month, 74–94% at 6 months, 70–81% at 12 months, 81–90% at 2–5 years, and up to 94% at 10 years in non-functioning solid nodules. (37–40)

## 2. Symptom and cosmetic improvement

RFA significantly improves symptom and cosmetic scores. Mean symptom scores decrease from approximately 3.83 to 1.09 on a 10-point scale, while cosmetic scores decrease from 3.43 to 1.51 on a 4-point scale. These improvements are sustained even in studies with long-term follow-up. (37–40)

## PART 2: RADIOFREQUENCY ABLATION (RFA) FOR AUTONOMOUSLY FUNCTIONING THYROID NODULES (AFTN)

### Recommendation 2.1 (Strong recommendation)

RFA may be indicated by a multidisciplinary team (endocrinologist, nuclear medicine physician, surgeon, and interventional radiologist) for autonomously functioning thyroid nodules (AFTNs) or pre-toxic nodules (causing subclinical hyperthyroidism) with a volume  $\leq 20$  mL in elderly patients, in patients with hyperthyroid symptoms, cosmetic concerns, or compressive symptoms who refuse surgery or are not suitable surgical candidates, and in those who refuse or fail radioactive iodine (RAI) therapy and other medical treatments.

AFTNs may be treated in the presence of compressive symptoms, cosmetic concerns, overt hyperthyroidism, and pre-toxic nodules. Current American Thyroid Association guidelines suggest that two effective and relatively safe definitive treatment options for toxic AFTNs are radioactive iodine (RAI) therapy and surgery. (41) However, hypothyroidism after surgery or RAI may complicate pre-existing chronic diseases in elderly patients and remains controversial in young women. (42) Moreover, some patients refuse RAI therapy or surgery because they wish to avoid radiation exposure or potential complications such as hypothyroidism. As an alternative, RFA for AFTNs has been reported in recent studies. (43,44) An Italian group suggested that hyperthyroidism due to AFTN can be completely or partially resolved by RFA when surgery and RAI therapy are contraindicated or refused. (45)

In addition, pre-toxic nodules—characterized by normal thyroid hormone levels with low TSH—are also often recommended for treatment because they may progress to overt toxic nodules (annual risk, approximately 4%); furthermore, subclinical hyperthyroidism may have adverse effects over time, particularly on the skeletal and cardiovascular systems. (46)

*RFA is less effective for large AFTNs (volume >20 mL) and is currently not strongly recommended for this subgroup. (46)*

### Recommendation 2.2 (Strong recommendation)

Pre-procedural evaluation for RFA of toxic or pre-toxic AFTNs should include:

- (i) thyroid scintigraphy;
  - (ii) thyroid function tests (TSH and FT4);
  - (iii) confirmation of benignity by at least one FNA or CNB (after achieving euthyroid status);
  - (iv) assessment of nodule size, volume, cosmetic score, symptom score, and intranodular vascularity; and
  - (v) informed consent obtained prior to the procedure.
- (i) Thyroid scintigraphy

Thyroid scintigraphy is an essential step recommended to confirm the presence of an autonomously functioning nodule. These nodules are often referred to as “hot nodules,” and confirmation of autonomous hyperfunction is necessary because treatment outcomes may differ across nodule types. When clinical hyperthyroidism is suspected, thyroid scintigraphy using technetium-99m pertechnetate or iodine-131 may be performed. On follow-up scintigraphy, thyroid nodules can be classified into three categories: type 1—hot nodule; type 2—uptake similar to surrounding thyroid tissue; and type 3—cold nodule or non-visualized status. (29,42)

(ii) Thyroid function tests

Toxic nodules are characterized by hyperthyroidism. Achieving euthyroid status before FNA/CNB and subsequently before RFA is crucial to optimize procedural efficacy and, more importantly, to prevent complications, including cardiovascular (tachycardia, arrhythmia), neurologic (restlessness, anxiety), and particularly severe complications such as thyroid storm. The preparation period is typically 4–8 weeks, depending on severity. The KSThR 2025 recommendations advise rechecking FT4 after 4 weeks to confirm euthyroid status. Basic coagulation and platelet testing should be performed similarly to RFA for benign nodules.

(iii) Cytologic or histologic confirmation

A single benign diagnosis on FNA or CNB is sufficient to confirm the benignity of a hot thyroid nodule. Although case reports of malignant AFTNs have been described, (49) AFTNs are predominantly benign lesions. (16,24) Therefore, a single benign FNA or CNB result is

recommended to confirm benignity of the hot nodule prior to RFA.

(iv) Ultrasound assessment

Nodule size, volume, intranodular vascularity, cosmetic score, and compressive symptom scores should be evaluated in the same manner as for benign thyroid nodules.

(v) Informed consent checklist

Patients should be informed that:

1. Treated nodules gradually decrease in size over months to years:
  - At 1 month: volume reduction of 36.4% to 51%
  - At 6 months: volume reduction of 69% to 74.5%
  - At 12 months: approximately 75% volume reduction
2. Thyroid functional outcomes: normalization occurs in 45–80% of cases and is higher in smaller nodules.
3. The expected number of treatment sessions depends on hyperthyroidism severity and nodule recurrence.
4. The risk of regrowth and the potential need for additional hormonal therapy:
  - Regrowth risk may be higher in hot nodules than in cold nodules due to richer vascularity and higher marginal recurrence.
  - The need for supplemental hormone therapy may occur depending on thyroid function changes.
5. Patients may experience varying degrees of pain during the procedure.
6. Potential complications of RFA.
7. Patients should inform physicians of any history of thyroid surgery, adverse effects of any current medications, and whether they are taking antiplatelet agents, anticoagulants, or thyroid hormone.
8. Additional observation or hospitalization may be required depending on patient condition after treatment.

### Recommendation 2.3 (Strong recommendation)

Appropriate techniques for RFA of hot thyroid nodules include:

- (i) perithyroidal local anesthesia with lidocaine;
- (ii) hydro dissection;
- (iii) the trans isthmic approach;
- (iv) the moving-shot technique;
- (v) appropriate electrode selection; and
- (vi) continuous real-time ultrasound monitoring.

RFA techniques for AFTNs are fundamentally similar to those used for benign thyroid nodules. However, the moving-shot technique is preferred, with particular emphasis on maximizing treatment of the marginal area, and vascular ablation techniques should be considered to reduce marginal regrowth.

### Recommendation 2.4 (Strong recommendation)

Post-procedural evaluation after RFA should include:

- (i) thyroid function tests (TSH and FT4);
  - (ii) nodule size, volume, cosmetic score, and symptom score; and
  - (iii) intranodular vascularity.
- (i) Clinical, laboratory, and imaging follow-up

After RFA for AFTN, clinical assessment, laboratory testing, and imaging follow-up are required. Thyroid function should be monitored at each follow-up visit by measuring TSH and FT4. (23,44,47) Based on TSH changes, antithyroid drugs may be tapered or discontinued. Treatment response is classified into three categories depending on medication requirement: remission (euthyroid status after discontinuation of antithyroid drugs), improvement (dose reduction to achieve euthyroid status), and non-response (no change in dose compared with baseline). (44)

Measurement of thyroid autoantibodies (anti-TPO and anti-Tg) is necessary in selected cases. After RFA, patients with elevated autoantibodies may develop subclinical hypothyroidism. (34) Therefore, if thyroid autoantibodies are elevated before RFA, thyroid function should be monitored carefully during follow-up. In patients with normal baseline autoantibodies, newly elevated thyroid antibodies during follow-up are rare. If serum TSH receptor antibodies are elevated before RFA, concomitant Graves' disease and AFTN may be present, and post-RFA hormonal changes may be incomplete

even after technically successful ablation. (34,35,48)

Neck ultrasound should be performed at each follow-up visit to assess changes in nodule size, volume, vascularity, and echogenicity. If thyroid function or symptoms are not fully resolved, repeat RFA or alternative therapies such as medication may be required. Repeat RFA may be determined based on serum TSH rather than scintigraphy findings or residual viable tissue on ultrasound. Rarely, because complete ablation of hot nodules may lead to hypothyroidism, additional ablation should be decided cautiously according to serum TSH changes.

Repeat RFA may be suggested during follow-up when serum TSH does not return to normal after the first RFA session. Repeat RFA can be considered 1–3 months after the initial procedure because nodule volume decreases rapidly during the first 3 months after RFA. (42) Previous studies reported a mean number of treatment sessions of 1.8–2.2 (range, 1–6 sessions) for AFTNs. (29,42)

#### **Recommendation 2.5 (Weak recommendation)**

Efficacy of RFA for AFTNs includes volume reduction (53–85%) within 1 month to 1 year and normalization of thyroid function (24–82%).

The efficacy of RFA in AFTNs has been reported with VRRs ranging from 53% to 85%, while the thyroid function normalization rate varies widely (24%–82%). (8,32,42,47,49,50) A single RFA session reduced nodule volume by 36.4%–51%, 69%–74.5%, and 75% at 1, 6, and 12 months, respectively. (44,51) Volume reduction is closely associated with significant improvement in neck discomfort and cosmetic concerns. (53)

The response of hot nodules to RFA is generally lower than that of cold nodules because hot nodules show richer vascularity and higher marginal recurrence rates. (29,42) However, one study reported that hot nodules demonstrated a slightly greater response than cold nodules ( $52.1 \pm 16.2\%$  vs  $46.2 \pm 16.9\%$  volume reduction, respectively). (8)

A single RFA session allowed discontinuation of antithyroid drugs in 21.7%–50% of patients. (9,46) Methimazole dosage was reduced after RFA in 78% of patients. (9) Regarding thyroid function outcomes, 33% of patients achieved remission at 3 months, 43%–50% at 6 months, and 50% at 12 months after RFA. (44) Serum TSH returned to normal in 55.6%–81.8% of patients at the last follow-up. (29,42) One study reported that hyperthyroidism was completely controlled in 24% of patients and partially improved in the remaining patients. (9) On scintigraphy, most hot nodules (44.4%–79.5%)

became cold or normal; 20.4%–55.6% showed decreased uptake although they remained hot nodules. (35,44)

Variability in treatment outcomes across studies may be attributed to residual viable tissue at the nodule margin, which can result in insufficient volume reduction and persistent hyperthyroidism. (35,44) The moving-shot technique and internally cooled electrodes may represent a safe approach for marginal ablation. A recent multicenter retrospective study performed by trained radiologists using the moving-shot technique and similar devices (modified straight internally cooled electrodes) demonstrated improvement of hyperthyroidism in all patients, with a VRR of 81.7%, a TSH normalization rate of 81.8%, and scintigraphy normalization in 79.5%. (44)

For large AFTNs (typically >20 mL), RFA is less effective. (29,45,49) Although not fully established in the literature, combined treatment with RFA and RAI therapy may be investigated in the future. RFA is an effective non-surgical option to improve thyrotoxic symptoms, hormone levels, and scintigraphic findings in the management of AFTNs; however, the number of studies remains limited and results are heterogeneous.

### **PART 3: RADIOFREQUENCY ABLATION (RFA) FOR PAPILLARY THYROID CARCINOMA**

#### **Recommendation 3.1 (Weak recommendation)**

RFA may be indicated by a multidisciplinary team (endocrinologist, nuclear medicine/oncology physician, surgeon, and interventional radiologist) for low-risk papillary thyroid carcinoma (PTC) in elderly patients (>60 years), patients with significant comorbidities and high surgical risk who are not candidates for surgery, and patients who refuse surgical treatment or active surveillance.

- Indications (applicable to patients with confirmed low-risk PTC, defined by concordance between high-suspicion ultrasound findings (TIRADS 4–5) and cytology (FNA) or core-needle biopsy (CNB), and meeting all of the following criteria) (52):
  - Maximum tumor diameter  $\leq 1$  cm.
  - Solitary tumor.
  - No invasion of the trachea, major neck vessels, or other perithyroidal structures.
  - No evidence of cervical lymph node metastasis (on ultrasound and contrast-enhanced neck CT).

- No evidence of distant metastasis.
- Relative indications (may be considered depending on available technical and medical resources, for biopsy-proven PTC without cervical lymph node or distant metastasis (cN0M0) and meeting any of the following criteria):
  - Tumor located in the isthmus.
  - Tumor adjacent to the capsule or with suspected capsular invasion on ultrasound.
  - Maximum tumor diameter >1 cm and ≤2 cm.
  - Multifocal tumors (≤3 lesions, with maximum diameter ≤1 cm).

RFA may be considered for patients who cannot tolerate surgery due to comorbidities or who refuse surgery for various reasons.

Surgery remains the standard treatment for primary thyroid cancer, particularly in younger patients (<40 years). Therefore, indications for RFA in primary thyroid cancer have not been clearly established. However, in patients with primary thyroid cancer who refuse surgery or are not candidates for surgery, RFA may be considered as an alternative option. Recently, RFA has been investigated for papillary thyroid microcarcinoma (PTMC). These studies reported favorable short-term local tumor control and outcomes during follow-up up to 4 years. (53–57)

In addition, palliative treatment is another option for advanced thyroid cancer. Several reports have described palliative treatment of advanced anaplastic thyroid carcinoma or medullary thyroid carcinoma using RFA or laser ablation (LA). (58–61)

### Recommendation 3.2 (Weak recommendation)

Pre-procedural evaluation for RFA of PTC should include:

- (i) confirmation of PTC by FNA or CNB before RFA;
- (ii) ultrasound assessment of tumor size, volume, intranodular vascularity, and the relationship between the tumor and adjacent structures;
- (iii) neck ultrasound and contrast-enhanced neck CT to evaluate cervical lymph node metastasis, and chest CT to evaluate distant metastasis;
- (iv) thyroid function tests (TSH and FT4); and
- (v) informed consent obtained prior to the procedure.

When thyroid nodules are classified as “high risk” (TIRADS 4 or 5) on ultrasound, FNA or CNB should be performed if the nodule diameter is >1 cm. For smaller nodules (>0.5 cm and ≤1 cm), FNA/CNB should be considered if:

1. Progression is observed during follow-up; or
2. The nodule has an ill-defined interface with the trachea or posterior thyroid capsule along the expected course of the recurrent laryngeal nerve (because these may represent cancers with unfavorable prognostic features requiring treatment). (62–64)

A careful ultrasound assessment of the relationship between the tumor and critical neck structures (including the trachea, vessels, esophagus, and recurrent laryngeal nerve) should be performed to determine the optimal needle trajectory. (53)

### Cervical lymph node assessment

Neck ultrasound should evaluate lymph nodes in the central and lateral neck compartments (levels II, III, IV, V, and VI), with risk stratification based on the 2025 KTA/KSThR guideline on active surveillance for PTMC.

### Classification – Imaging Features – Estimated Malignancy Risk – FNA Criteria

#### Suspicious

- US: Presence of any of the following:
  - Cystic change
  - Echogenic foci / calcifications
  - Hyperechogenic cortex (focal or diffuse)
  - Abnormal vascularity (peripheral or diffuse)
- CT: Presence of any of the following:
  - Cystic change
  - Calcifications
  - Strong (focal/diffuse) or heterogeneous enhancement
- Estimated malignancy risk: 73–88%
- FNA indication: Short-axis diameter >3–5 mm

#### Indeterminate

- US: Loss of echogenic hilum without other suspicious features
- CT: Loss of fatty hilum without other suspicious features
- Estimated malignancy risk: ~20%

- FNA indication: Short-axis diameter >5 mm

Probably benign

- US: Presence of echogenic hilum or hilar vascularity and no suspicious features
- CT: Presence of fatty hilum or hilar enhancement and no suspicious features
- Estimated malignancy risk: <3%
- FNA indication: Not applicable

Ultrasound-guided FNA should be performed for suspicious lymph nodes, combined with measurement of thyroglobulin (Tg) in the needle washout (in 1 mL normal saline). Lymph node metastasis is confirmed when Tg in the washout fluid is higher than the serum Tg level or exceeds 1 ng/mL. (65)

Distant metastasis assessment before RFA (66)

CT of the chest and abdomen should be performed to evaluate pulmonary and osseous metastasis. Although the lung is the second most common site of distant metastasis after lymph nodes, the rate of distant metastasis in PTMC is extremely low (<0.1%). (67)

(v) Informed consent checklist

Patients should be informed that:

1. Surgery is the standard recommended treatment according to current guidelines.
2. Treated thyroid tumors gradually decrease in size over months to years.
3. RFA cannot eliminate the risk of PTMC recurrence or cervical lymph node metastasis.
4. Patients may experience varying degrees of pain during the procedure.
5. Potential complications of CNB and RFA.
6. Patients should inform physicians of any history of thyroid surgery, adverse effects of any current medications, and whether they are taking antiplatelet agents, anticoagulants, or thyroid hormone therapy.
7. Additional observation or hospitalization may be required depending on patient condition after treatment.

### Recommendation 3.3 (Strong recommendation)

Appropriate techniques for RFA of PTC include:

- (i) perithyroidal local anesthesia with lidocaine;

- (ii) hydro dissection;

- (iii) the trans isthmic approach and moving-shot technique;

- (iv) establishment of a safety margin; and

- (v) appropriate electrode selection, energy control, and real-time monitoring.

- (i) Local anesthesia with 1% lidocaine should be administered at the skin puncture site and the anterior thyroid capsule.

- (ii) Hydro dissection: If the distance between the tumor and critical neck structures (including the trachea, carotid artery, internal jugular vein, esophagus, and recurrent laryngeal nerve) is <5 mm, 5% dextrose solution should be injected using a separate needle to create a distance of at least 1 cm to prevent thermal injury. The initial injected volume is 5–10 mL and can be increased up to 20 mL as needed.

- (iv) Safety margin: A safety margin of 3–5 mm beyond the tumor margin should be included to reduce the risk of residual tumor and recurrence. (68,69)

- (v) Electrode selection: Electrode active-tip size should be selected based on tumor size and proximity to critical structures. Small active tips (0.38 cm or 0.5 cm) are effective and safe for treating primary tumors.

Energy control: During ablation, the generator continuously measures tissue impedance between electrodes at the active tip. Energy is automatically reduced if the electrode temperature reaches 100°C, causing a characteristic rise in tissue impedance.

Power settings:

- Initial power: 3 W.
- If a transient hyperechoic zone does not form at the electrode tip within 5–10 seconds, power is increased to 5 W. (53)

Ablation endpoint: Ablation should be terminated when the entire tumor and safety margin become a transient hyperechoic zone.

### Recommendation 3.4 (Strong recommendation)

Post-procedural evaluation after RFA should include:

- (i) tumor size, volume, and intranodular vascularity; (ii) thyroid function tests (TSH and FT4); and (iii) neck ultrasound and contrast-enhanced neck CT.

After RFA for malignant thyroid nodules, endocrinologists should implement TSH suppression therapy. The target

TSH level should be determined based on the initial risk of recurrence, potential adverse effects of TSH suppression, and the patient's treatment response. Several studies have reported an association between TSH level and tumor progression risk: higher TSH levels (>2 mIU/L) are significantly associated with an increased risk of tumor progression (tumor growth, lymph node metastasis). (70)

Data on the use of RFA for primary thyroid cancer remain limited, and post-procedural surveillance strategies are controversial in previous reports. (53,54) In a prospective study by Zhang et al. (73), patients were followed at 1, 3, 6, and 12 months after RFA using ultrasound and contrast-enhanced ultrasound; FNA/CNB was performed at 3 months after RFA in each patient. (73) In a study by Kim et al. (74), post-procedural ultrasound was performed at 1, 6, and 12 months and annually thereafter.

As in patients undergoing thyroid lobectomy for cancer and in those receiving RFA for recurrent thyroid cancer, ultrasound is recommended primarily to evaluate the ablation zone. In addition, careful assessment is required to detect synchronous PTC developing in other regions of the thyroid gland and newly appearing lymph node metastasis. CT appears to play an important complementary role in detecting newly developed lymph node metastasis. As described in previous studies, size reduction of the post-ablation lesion typically represents degenerative changes; CNB or FNA is recommended only for lesions that increase in size or remain unchanged. (73,74)

#### **Recommendation 3.5 (Strong recommendation)**

RFA is not recommended for papillary thyroid carcinoma (PTC) with any of the following features: multifocal PTC (>4 tumors), suspected cervical lymph node or distant metastasis, definite extrathyroidal extension or invasion of the trachea/esophagus, diffuse sclerosing variant of PTC, or malignancies other than PTC.

#### **Recommendation 3.6 (Weak recommendation)**

Current evidence suggests that RFA for selected low-risk PTC is effective with a low complication rate and may be considered as an alternative to surgery in carefully selected patients.

A meta-analysis of 36 studies reported a complete tumor disappearance rate of 91% (CI, 83–97%) for cT1a PTC and 60% (CI, 50–70%) for cT1b PTC. (71)

Zhang et al. (73) reported prospective but short-term follow-up (mean, 7.8 months). They treated 98 PTMCs in 92 patients and reported mean residual volume ratios of  $0.47 \pm 0.27$ ,  $0.19 \pm 0.16$ ,  $0.08 \pm 0.11$ ,  $0.04 \pm 0.10$ , and

0 at 1, 3, 6, 12, and 18 months, respectively, after RFA. Four patients reported transient voice-related complaints.

A long-term follow-up study (mean, 48 months) in six patients reported a mean VRR of  $98.5 \pm 3.3\%$ , with complete disappearance of tumors on ultrasound in four cases. (74) No local tumor recurrence or metastatic lesions were observed during follow-up in both short- and long-term studies.

However, a case report describing outcomes of three low-risk PTC patients who underwent surgery after laser ablation (LA) (55) showed that LA provided local tumor control of the primary cancer, but bilateral microscopic tumors and micro-metastases in central lymph nodes were detected at surgery. Therefore, thermal ablation may be effective for local management of primary thyroid cancer but appears limited in controlling regional micro-metastasis or small multifocal cancers. Further studies are required.

## **PART 4: RADIOFREQUENCY ABLATION (RFA) FOR RECURRENT THYROID CARCINOMA (RTC)**

### **Recommendation 4.1 (Strong recommendation)**

RFA may be indicated by a multidisciplinary team (endocrinologist, nuclear medicine physician, surgeon, and interventional radiologist) with curative or palliative intent for recurrent thyroid carcinoma in the thyroid bed and cervical lymph nodes in patients with high surgical risk or those who refuse surgery, including patients with RAI-refractory disease.

#### **Curative intent**

- Considered when complete tumor eradication is achievable.
- Typically indicated for RTC with a limited number of lesions ( $\leq 4$ ) and small tumor size ( $\leq 2$  cm).
- No evidence of distant metastasis.

For RTC in the lateral neck in patients without high surgical risk, neck dissection remains the primary treatment option.

Studies have demonstrated favorable local control of RTC in the central and lateral neck compartments after total thyroidectomy, with reported mean volume reduction ratios (VRR) of 81.2% to 98.4% and complete disappearance rates of 61.1% to 100%.

#### **Palliative intent**

- RFA may be used when tumor volume reduction

is expected to alleviate symptoms and improve quality of life.

- It may be considered for larger tumors.
- Even in cases with airway invasion, RFA remains a feasible option for local control of RTC in the central compartment.

When recurrent thyroid carcinoma is detected, surgery followed by RAI therapy and thyroid hormone therapy is considered standard treatment. However, repeat neck surgery is often challenging due to altered anatomy and postoperative scar-related fibrosis, leading to a higher risk of complications. (72) With population aging, the number of elderly patients requiring treatment for RTC yet carrying high operative risk is increasing. In addition, some patients refuse repeat surgery. For these reasons, management of RTC in patients who are difficult surgical candidates is an important clinical issue.

In 2001, Dupuy et al. (72) first reported RFA for recurrent papillary and follicular thyroid carcinoma in eight patients. Subsequently, multiple studies—including two meta-analyses—have reported RFA for recurrent thyroid carcinoma. (36,73–76) In these reports, indications for RFA included RTC patients at high surgical risk or those refusing surgery despite having clinically relevant disease requiring treatment. High surgical risk includes prior repeat surgery, poor pulmonary function, poor general condition, severe cardiovascular disease, or advanced age. RFA may be performed with curative intent or for palliation. For curative treatment, RFA should be applied only when imaging suggests that complete ablation is feasible and when there is no distant metastasis. Favorable outcomes have been reported in recent studies using curative-intent RFA in patients with fewer than four locally recurrent lesions and maximum lesion diameter <2 cm. (36,77,78)

RTC can cause symptoms such as dysphagia, hoarseness, dyspnea, or cosmetic deformity due to protruding masses. RFA may be applied when tumor reduction is expected to relieve symptoms and improve quality of life even when complete eradication is not feasible. (75) In contrast to repeat surgery, which may be limited and complicated by fibrosis and distorted normal anatomy, RFA can often treat recurrent tumors successfully without significant complications. (78)

#### **Recommendation 4.2 (Strong recommendation)**

Pre-procedural evaluation before RFA for RTC lesions in the thyroid bed and cervical lymph nodes should include:

- (i) confirmation of RTC by FNA or CNB;

- (ii) ultrasound and contrast-enhanced neck CT for diagnosis, localization, lesion count, and assessment of size and relationships to adjacent structures;
- (iii) assessment of tumor vascularity pattern;
- (iv) serum thyroglobulin (Tg), anti-thyroglobulin antibody (Tg-Ab), and serum TSH; and
- (v) informed consent obtained prior to the procedure.

RTC commonly occurs in the thyroid bed or cervical lymph nodes, with a recurrence rate of approximately 10–30% in differentiated thyroid cancer (DTC).

Before RFA for recurrent thyroid cancer, recurrence should be confirmed by ultrasound-guided FNA with measurement of Tg in needle washout fluid. (36,62,79)

**FNA (fine-needle aspiration):** Ultrasound-guided cytology to confirm recurrence in the thyroid bed or cervical lymph nodes. Tg washout improves sensitivity (Tg >1 ng/mL suggests recurrence). **CNB:** If FNA is insufficient, CNB can be performed to obtain a larger tissue sample.

**Serum thyroglobulin (Tg):** Tg is the primary biomarker for DTC recurrence. Elevated Tg (>1 ng/mL) after total thyroidectomy suggests recurrence. According to ATA recommendations, Tg should be interpreted together with anti-Tg to avoid false results. If Tg is elevated, imaging (ultrasound and contrast-enhanced neck CT) is required to localize RTC.

#### **Neck ultrasound**

Neck ultrasound is the first-line and most sensitive modality for detecting recurrence in the thyroid bed and cervical lymph nodes. Ultrasound is critical for characterizing recurrent tumors, carefully evaluating adjacent critical anatomy (nerves, trachea, esophagus, vessels), and assessing tumor vascularity. It is the primary imaging modality for RFA guidance and post-procedural follow-up.

- Thyroid bed recurrence: Irregular mass, increased vascularity, or calcifications.
- Cervical lymph node recurrence: Enlarged nodes (>1 cm), round shape, loss of nodal hilum, increased vascularity, or calcifications.

#### **Tumor vascularity**

Tumor vascularity (neovascularization) of recurrent thyroid carcinoma has several implications:

- Pre-procedural planning: Vascularity should be carefully assessed on ultrasound during

preparation, as part of tumor characterization and treatment planning.

- Indicator of technical success: Disappearance of intratumoral vascularity after RFA is considered a criterion of technical success, particularly for curative intent. Successfully ablated tumors typically decrease in size, lose intratumoral vascularity, and show hyperechoic changes on follow-up ultrasound.
- Treatment challenge and recurrence risk: High vascularity may adversely affect RFA outcomes and be associated with higher marginal recurrence, similar to benign nodules, suggesting a higher risk of incomplete ablation and recurrence.

Neck CT with a dedicated thyroid protocol is recommended to identify recurrent tumors not detected by ultrasound and may be useful for evaluating recurrence after RFA. PET/CT or scintigraphy: 18F-FDG PET/CT may be used for DTC recurrence when Tg is positive but ultrasound is negative, particularly in high-risk patients. I-131 whole-body scintigraphy can be used to assess iodine uptake.

#### (v) Informed consent checklist

Patients should be informed about:

1. The intent of RFA (curative vs palliative).
2. The expected number of treatment sessions.
3. The risk of tumor recurrence and disease progression.
4. Potential pain during the procedure.
5. Potential complications of RFA.
6. The need to report prior thyroid surgery and current medications (antiplatelets, anticoagulants, thyroid hormone).
7. The possibility of additional observation or hospitalization after treatment depending on patient condition.

#### **Recommendation 4.3 (Strong recommendation)**

Appropriate techniques for RFA of RTC lesions in the thyroid bed and cervical lymph nodes include:

- (i) perilesional local anesthesia with lidocaine;
- (ii) hydro dissection;
- (iii) the moving-shot technique or fixed-electrode technique;
- (iv) electrode selection;

(v) energy control; and

(vi) continuous real-time ultrasound monitoring.

For RFA of recurrent thyroid carcinoma, perilesional lidocaine injection, hydro dissection, and the moving-shot technique are recommended as standard techniques.

#### (i) Local anesthesia

Perilesional lidocaine injection is generally sufficient for pain control during RFA for RTC.

#### (ii) Hydro dissection

Hydro dissection uses cold 5% dextrose water (D5W) to separate the tumor from adjacent critical structures. This is essential to prevent thermal injury to the recurrent laryngeal nerve, middle cervical sympathetic ganglion, brachial plexus, phrenic nerve, as well as the trachea and esophagus. Careful monitoring of the distance between nerves and the electrode tip is required. Cold D5W injection may also help relieve neurologic symptoms if nerve injury occurs. Hydro dissection is also effective in preventing skin burns when RTC involves the skin.

Unlike benign nodules, recurrent tumors after surgery often abut critical structures such as the recurrent laryngeal nerve or trachea; therefore, careful assessment of the tumor and adjacent anatomy is essential before ablation. (80) Hydro dissection is useful for separating the tumor from critical structures in addition to perilesional lidocaine injection for analgesia. (23,78,81) D5W is preferred over normal saline because saline is ionic and thus electrically conductive. (82) Continuous injection of cold D5W through a needle maintained in position can create a safety space and reduce heat propagation to adjacent structures during the procedure. (24)

#### (iii) Ablation technique

The moving-shot technique has been proposed as an appropriate technique for RTC ablation, including the peritumoral soft tissue around recurrent lesions. (24,78)

Fixed-electrode technique: May be used for very small tumors (<5 mm), in which the electrode is kept fixed at the tumor center during ablation.

Safety margin: If feasible, RFA should include both the metastatic tumor and adjacent normal tissue with a safety margin of approximately 1–2 mm to prevent marginal recurrence.

Ablation endpoint: Ablation is terminated when all portions of the tumor become transient hyperechoic zones on ultrasound. Complete devascularization and disappearance of abnormal vasculature immediately

after RFA-assessed using Doppler or contrast-enhanced ultrasound (CEUS)-is a criterion for technical success in curative-intent procedures.

(v) Electrode selection

Modified straight, internally cooled electrodes that are shorter (7 cm) and thinner (18–19 G) than conventional electrodes are commonly used for RTC ablation. Active-tip size is selected according to tumor size and proximity to critical structures. Small active tips (0.38 cm or 0.5 cm) are effective and safe for small primary and/or recurrent tumors or tumors near critical structures. (24) Bipolar electrodes have recently been introduced for patients with cardiac conditions or for pregnant women. (30)

Energy control and power settings

During ablation, the generator continuously measures tissue impedance; energy is automatically reduced when electrode temperature reaches 100°C, producing a characteristic rise in impedance.

Power settings:

- Initial power: 10 W.
- If a transient hyperechoic zone does not form at the electrode tip within 5–10 seconds, power is increased in 5-W increments up to a maximum of 40 W. (36)

Ablation endpoint: When the entire lesion and safety margin have become a transient hyperechoic zone.

(vi) Continuous monitoring

Electrode tip position must be continuously monitored using real-time ultrasound throughout the procedure. Advanced Doppler techniques (e.g., microvascular flow imaging, Micro-Flow Imaging, superb microvascular imaging, slow-flow imaging) and CEUS are useful for detecting abnormal tumor vasculature and assessing technical success immediately after RFA.

**Recommendation 4.4 (Strong recommendation)**

Post-procedural evaluation after RFA for RTC in the thyroid bed and cervical lymph nodes should include:

- tumor size, volume, cosmetic score, and symptom score;
- tumor vascularity; and
- thyroid function tests (TSH and FT4) as well as serum Tg and anti-Tg.

After RFA of recurrent neck tumors, routine ultrasound follow-up is recommended at 1 (or 2), 3, and 6 months,

and then every 6 months depending on the treated tumor status. Tumor volume, maximum diameter, vascularity, and development of new metastatic lesions should be assessed during follow-up. Immediately after RFA, tumor volume may increase due to edema and because the ablation zone is larger than the initial tumor (including the safety margin). Thereafter, volume decreases gradually, with the greatest reduction typically occurring during the first 1–3 months after RFA.

Serum Tg and anti-Tg should be carefully evaluated after ablation because serum Tg (half-life 3–4 days) decreases rapidly in most patients after ablation. (77,83) Anti-Tg should be measured concurrently with serum Tg, because anti-Tg can cause falsely low serum Tg values in immunoassays. (84) Anti-Tg may transiently increase after RFA as an immune response to the intervention and can also increase after RAI therapy. (67)

Contrast-enhanced neck CT-particularly early arterial phase imaging (20–25 seconds) with thin slices (<2.5 mm)-may be useful for assessing residual tumor or newly developed tumors. (78) After successful ablation, enhancement of the recurrent tumor disappears completely on CT. Additional ablation can be planned if follow-up ultrasound or CT demonstrates persistent Doppler signal or residual enhancing tumor.

**Recommendation 4.5 (Strong recommendation)**

RFA is an effective treatment for RTC, with reported mean VRR of 81.2%–98.4% and complete disappearance rates of 61.1%–100%; long-term disappearance (80 months) has been reported to reach 91.3%. (85) RFA appears particularly effective for small tumors ( $\leq 2$  cm) and a limited number of lesions ( $\leq 3$ ).

Since the first report by Dupuy et al. (86), multiple studies—including two meta-analyses-have reported ultrasound-guided RFA as a non-surgical treatment option for locally recurrent thyroid carcinoma. (36,72–74,77,78,83,87) These meta-analyses concluded that RFA results in significant reductions in tumor volume, maximum diameter, and serum Tg levels in locally recurrent thyroid carcinoma. A meta-analysis by Suh et al. (83) reported a complete disappearance rate of 68.8%, a local recurrence rate at the treated site of 0%, and a serum Tg reduction rate of 71.6%. Reported tumor VRR ranged from 50.9% to 98.4%. (60,70)

In three studies restricting tumor size and number for curative-intent treatment of recurrent lesions (36,78,89), VRR ranged from 93% to 98.4% with no recurrence. Recurrence was defined as a new tumor or residual

tumor at the ablation site. (83) Kim et al. (78) reported 27 recurrent tumors treated with curative-intent RFA and compared RFA with repeat surgery using propensity score matching. The number of treated tumors was three or fewer and the maximum tumor diameter was <2 cm. After long-term follow-up (mean, 32.4 months), there were no significant differences between RFA and repeat surgery in recurrence rate, conversion to negative serum Tg, or 1- and 3-year recurrence-free survival.

RFA may be applied to relieve symptoms even when complete eradication is not feasible on imaging. Park et al. (75) reported symptom improvement in 63.6% of patients at 6 months in a short-term follow-up study of 16 recurrent tumors. However, in 62.5% of cases, technical incompleteness or failure occurred due to intolerable pain, heavy calcification, or tumors encasing major vessels. In such situations—large tumors, poor procedural tolerance, heavy calcification, or high-risk tumor location—additional RFA sessions may be required.

## PART 5: GENERAL IMPORTANT CONSIDERATIONS FOR RFA OF BENIGN AND MALIGNANT THYROID NODULES

### **Recommendation 5.1 (Strong recommendation)**

Thyroid RFA in general—particularly for autonomously functioning nodules, primary thyroid cancer, and recurrent thyroid carcinoma—should be performed by experienced thyroid-focused interventional physicians with formal training and should be conducted in multidisciplinary centers (endocrinology, oncology, head and neck surgery, interventional radiology, pathology, etc.) to maximize treatment efficacy and minimize post-procedural complications.

### **Recommendation 5.2 (Strong recommendation)**

Vocal cord function should be assessed before, during, and after thyroid RFA.

Voice change is the most common major complication after RFA. (67) The reported incidence is approximately 8% in RTC, higher than about 1% in benign thyroid nodules. The main cause is injury to the recurrent laryngeal nerve in the central compartment or the vagus nerve in the lateral neck. Potential mechanisms include direct thermal injury to the nerve or perineural hematoma formation. Therefore, assessment of vocal cord function is essential.

- Subjective voice assessment: A subjective voice evaluation should be performed before RFA

because voice change is the most common major complication of RFA. (67)

- Laryngeal examination: Because the incidence of voice change after RFA for RTC (especially central lesions) is higher than that for benign nodules, patients with a history of voice impairment or related surgery should undergo laryngeal assessment and evaluation of vocal cord mobility using endoscopy or ultrasound.
- Contralateral evaluation: Laryngeal examination should also be performed on the contralateral side before RFA.

### **Recommendation 5.3 (Strong recommendation)**

RFA is a safe minimally invasive procedure with a low complication rate.

Radiofrequency ablation is a safe treatment modality with a low complication rate when performed by experienced operators. Previous guidelines and studies, including meta-analyses, have demonstrated that RFA is safe with a low complication rate. (22,90–92) For benign nodules, the overall complication rate is 2.11% (95% CI, 1.15–3.06), and the major complication rate is 1.27% (95% CI, 0.81–1.73). For recurrent thyroid carcinoma, the overall complication rate is higher at 10.98% (95% CI, 4.82–17.15), and the major complication rate is 6.71% (95% CI, 3.05–10.36). (92)

A range of complications has been reported, including major complications such as nerve injuries (recurrent laryngeal nerve, cervical sympathetic ganglion, brachial plexus, and spinal accessory nerve), nodule rupture, and permanent hypothyroidism; and minor complications such as hematoma, vomiting, skin burns, transient thyrotoxicosis, lidocaine toxicity, hypertension, and pain. However, no life-threatening complications have been reported, and the sequela rate is 0.21%. (34,92,93)

Voice change, due to injury of the recurrent laryngeal nerve or the vagus nerve, is the most common major complication after RFA. The reported incidence is 1.45%, with permanent voice change in 0.17%. The incidence is higher in recurrent thyroid carcinoma (7.95%) than in benign thyroid nodules (0.94%). (34,92) Direct thermal injury to the nerve, nerve traction due to thyroid swelling, or nerve compression by hematoma may contribute to post-RFA voice change. (40,89,90) The trans-isthmus approach and the moving-shot technique are recommended to prevent recurrent laryngeal nerve injury. (108,112) In addition, anatomic variation or protruding nodules may shift the vagus nerve closer to the thyroid, increasing the risk of injury; therefore, operators should identify the

locations of the recurrent laryngeal nerve and vagus nerve.

Horner syndrome may occur due to thermal injury to the middle cervical sympathetic ganglion (mCSG). It presents as ptosis, miosis, and facial anhidrosis on the affected side. Conjunctival injection may be an early symptom of sympathetic ganglion injury. The mCSG is usually located at the lower thyroid level and may appear as a spindle-shaped hypoechoic structure adjacent to the common carotid artery (CCA). Medial to the CCA, the mCSG lies close to the thyroid and may be injured during RFA of benign nodules; lateral to the CCA, it may be vulnerable during RFA of recurrent tumors in the lateral neck. (112,147) Spinal accessory nerve injury and brachial plexus injury have also been reported during ablation. (100,144) Accordingly, ultrasound-based knowledge of neck anatomy is essential to prevent nerve injury, and areas potentially containing nerves should be treated with caution. If a metastatic tumor is adjacent to a nerve, hydro dissection with continuous fluid infusion may help prevent thermal injury. (108,112)

Nodule rupture is the detached second most common major complication (0.17%). It typically presents with sudden neck swelling and pain at the RFA site during follow-up. The mechanism has been attributed to acute volume expansion due to delayed hemorrhage or tearing of the nodule wall after neck massage. Ultrasound or CT typically shows thyroid capsule disruption with an anterior neck bulging mass. Most cases are managed conservatively with antibiotics and/or analgesics, but surgical treatment may be required if abscess formation occurs. (40,89)

Hematoma, caused by mechanical vascular injury from the electrode, may develop in perithyroidal spaces, beneath the capsule, or within the nodule. It is usually managed with simple neck compression for 30 minutes to 2 hours, and most hematomas resolve within 1–2 weeks. For prevention, perithyroidal vessels—including the superior and inferior thyroid arteries—should be carefully evaluated with Doppler ultrasound prior to electrode insertion. Severe bleeding can be prevented by careful monitoring of the electrode tip. (40,89,90)

Regarding thyroid function, hypothyroidism rarely occurs after RFA. A few reports describe hypothyroidism developing after RFA in patients with elevated anti-TPO antibodies before ablation or in patients with AFTN. (89,90) Transient hyperthyroidism can also occur after the procedure, but it usually resolves spontaneously within one month without symptoms. (40,89,90)

Pain is the most common complaint during RFA. Pain may vary in intensity in the lower neck and may radiate to the head, ear, shoulder, chest, back, or teeth. Although most patients tolerate pain and it decreases rapidly when generator power is reduced or temporarily stopped, some cases have been reported in which incomplete treatment occurred due to severe pain, requiring additional analgesics after RFA. (145) Analgesics may be prescribed for 2–3 days to relieve post-procedural pain in such cases. (10,89)

Life-threatening complications, including tracheal injury and esophageal rupture, have not been reported after thyroid RFA. Cough may be caused by heat spread to the trachea and can be managed by discontinuing ablation. To prevent thermal injury to the esophagus, patients may be instructed to swallow cold water while ablating units near the esophagus. (89)

For safe and effective procedures, operators must understand ultrasound-based neck anatomy, potential complications, and prevention techniques. Continuous and careful real-time ultrasound monitoring of the electrode tip is mandatory throughout the procedure.

Although there is no absolute contraindication to thyroid RFA, monopolar electrodes are not recommended in pregnant women or in patients with implanted electronic devices (e.g., pacemakers) due to insufficient evidence regarding safety. Bipolar electrodes may be a safer option in these patients, as electrical current is confined to the region around the active tip.

Overall, RFA is a safe method for treating benign thyroid nodules and recurrent thyroid carcinoma with a low complication rate. Ultrasound-based knowledge of neck anatomy and its clinical implications is essential for safe and effective ultrasound-guided RFA.

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