
بسم الله الرحمن الرحيم

Thermal Ablation for Papillary Thyroid Microcarcinomas PTMCs

Bijan Iraj,MD

Assistant Professor of Internal Medicine and Endocrinology
Department of Endocrinology and Metabolism
Isfahan Medical School

- The incidence of papillary thyroid carcinoma (PTC) and the number of these patients requiring subsequent surgery have markedly increased over the past 20 years. These increases are due primarily to the incidental detection of small, subclinical PTCs and/or early ultrasound screening.

- PTMC usually does not become clinically evident and is associated with an

excellent prognosis, either because the rate of progression is very slow or because the tumor does not progress.

- The American Thyroid Association guidelines suggested that an active surveillance can be considered in PTMC patients without local invasion or clinically evident metastases,

  and in patients who have high surgical risk, short remaining life span or concurrent medical issues requiring priority treatment.

- The indolent characteristics of PTC have reduced the need for immediate surgery, as surgery has several important drawbacks, including vocal cord paralysis, hypoparathyroidism, and post-surgical complications.

- Active surveillance (AS) is considered the alternative first-line option for patients with low-risk papillary thyroid microcarcinoma (PTMC), as it reduces overtreatment and unnecessary surgery, while showing favorable results, in these patients.

- According to a recent systematic review and meta-analysis, AS shows acceptable size enlargement and lymph node metastasis during 5 year follow-up (pooled proportion of 5.3% and 1.6%, respectively).

- Sakai T, Sugitani I, Ebina A, Fukuoka O, Toda K, Mitani H, Yamada K 2019 Active Surveillance for T1bN0M0 Papillary Thyroid Carcinoma. Thyroid : official journal of the American Thyroid Association **29:59-63.**

- Active surveillance can be an important management alternative for these patients. however, considering that over 10% of patients stopped active surveillance and underwent surgery without progression of disease in observational trials for PTMC.

- However, a large proportion (ranged 8.7 to 32 %) of patients underwent delayed surgery. Among them, a substantial proportion (ranging from 50 to 69%) of the reasons for delayed surgery were distinct from size enlargement or lymph node metastasis.

- Cho SJ, Suh CH, Baek JH, Chung SR, Choi YJ, Chung KW, Shong Y, Lee JH 2019 Active Surveillance for Small Papillary Thyroid Cancer: A Systematic Review and Meta-Analysis. Thyroid : official journal of the American Thyroid Association.

Anxiety is one of the main reasons for delayed surgery.

- Moreover, the tumor could evoke considerable patient anxiety when it is left untreated.

Active surveillance does not seem to be a perfect strategy for all patients.

- In recent years, image-guided ablations including ethanol injection, radiofrequency ablation (RFA) and microwave ablation

(MWA) have attracted much interest in the minimally invasive treatment of various tumors such as neoplasm's of the liver, kidney and lung.

- These techniques have been regarded as an alternative to surgery. Several studies

showed that RFA and MWA have been used to treat thyroid nodules and metastatic lymph nodes from PTC, yielding favorable results.

- Thermal ablation included MWA, LA, and RFA.

- US-guided laser ablation (LA) has also been demonstrated to be an effective method to reduce the volume of benign thyroid nodules , and to treat malignant diseases such as early hepatocellular carcinoma and metastatic lymph nodes from PTC.

- However, several recent studies have suggested the application of RFA for low-risk PMC

Kim et al. reported their indications as follows:

Pathologically confirmed PTC without cytological aggressiveness,

Single PTC without extrathyroidal extension,

No metastatic tumours

Ineligibility for surgery

Zhang M, Luo Y, Zhang Y, et al. (2016). Efficacy and safety of ultrasound-guided radiofrequency ablation for treating low-risk papillary thyroid microcarcinoma: a prospective study. Thyroid 26:1581–7.

Sun J, Liu X, Zhang Q, et al. (2016). Papillary thyroid carcinoma treated with radiofrequency ablation in a patient with hypertrophic cardiomyopathy: a case report. Korean J Radiol 17:558–61.

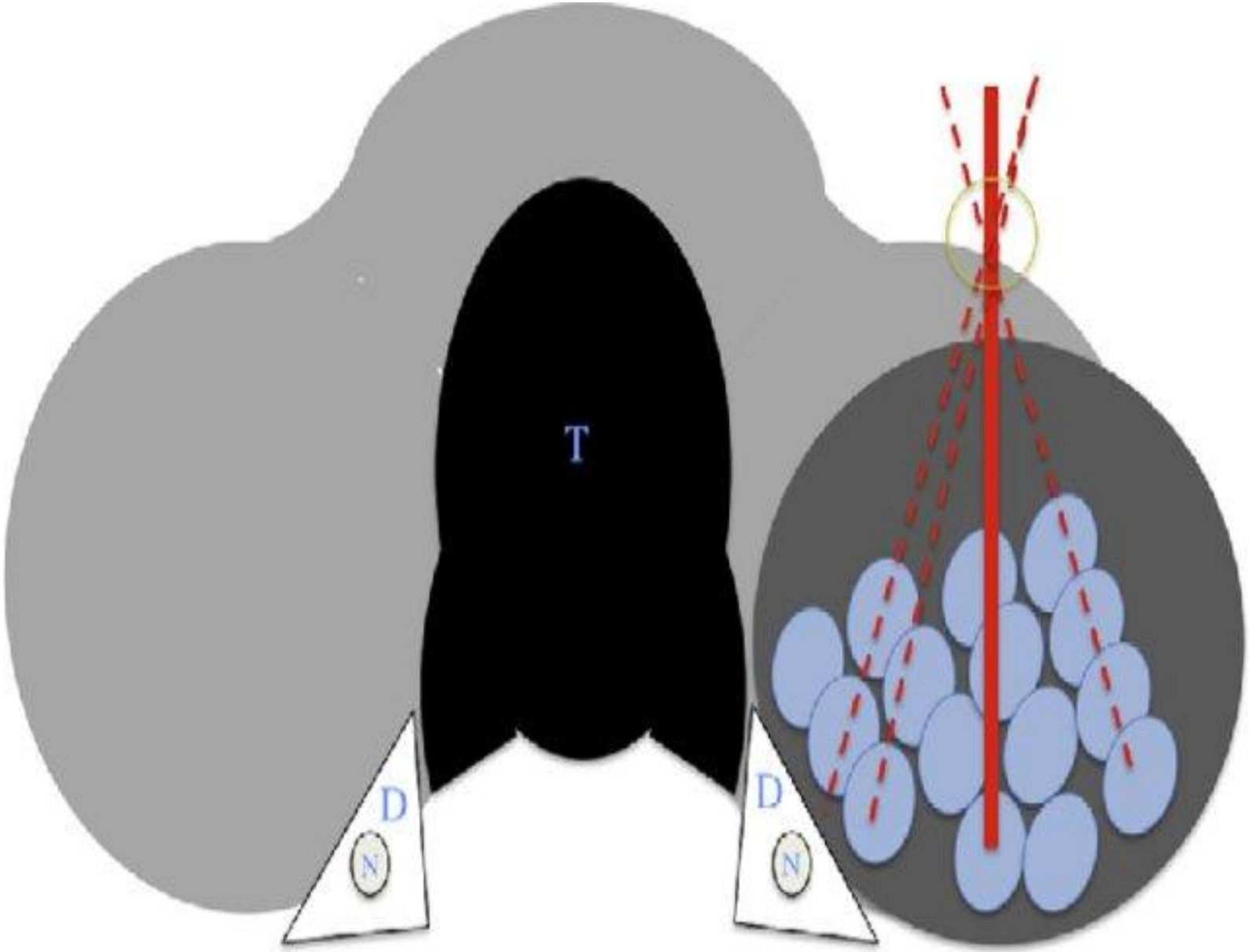
Kim JH, Baek JH, Sung JY, et al. (2017). Radiofrequency ablation of low-risk small papillary thyroidcarcinoma: preliminary results for patients ineligible for surgery. Int J Hyperthermia 33:212–19.

Techniques:

Before starting ablation, the target tumor is divided into multiple conceptual ablation units, and RFA is performed in a unit-by-unit manner by moving the electrode tip.

- The use of local anaesthesia rather than general anaesthesia or sedation.

- If a metastatic tumour exists adjacent to these nerves, the hydrodissection technique is useful to prevent thermal injury.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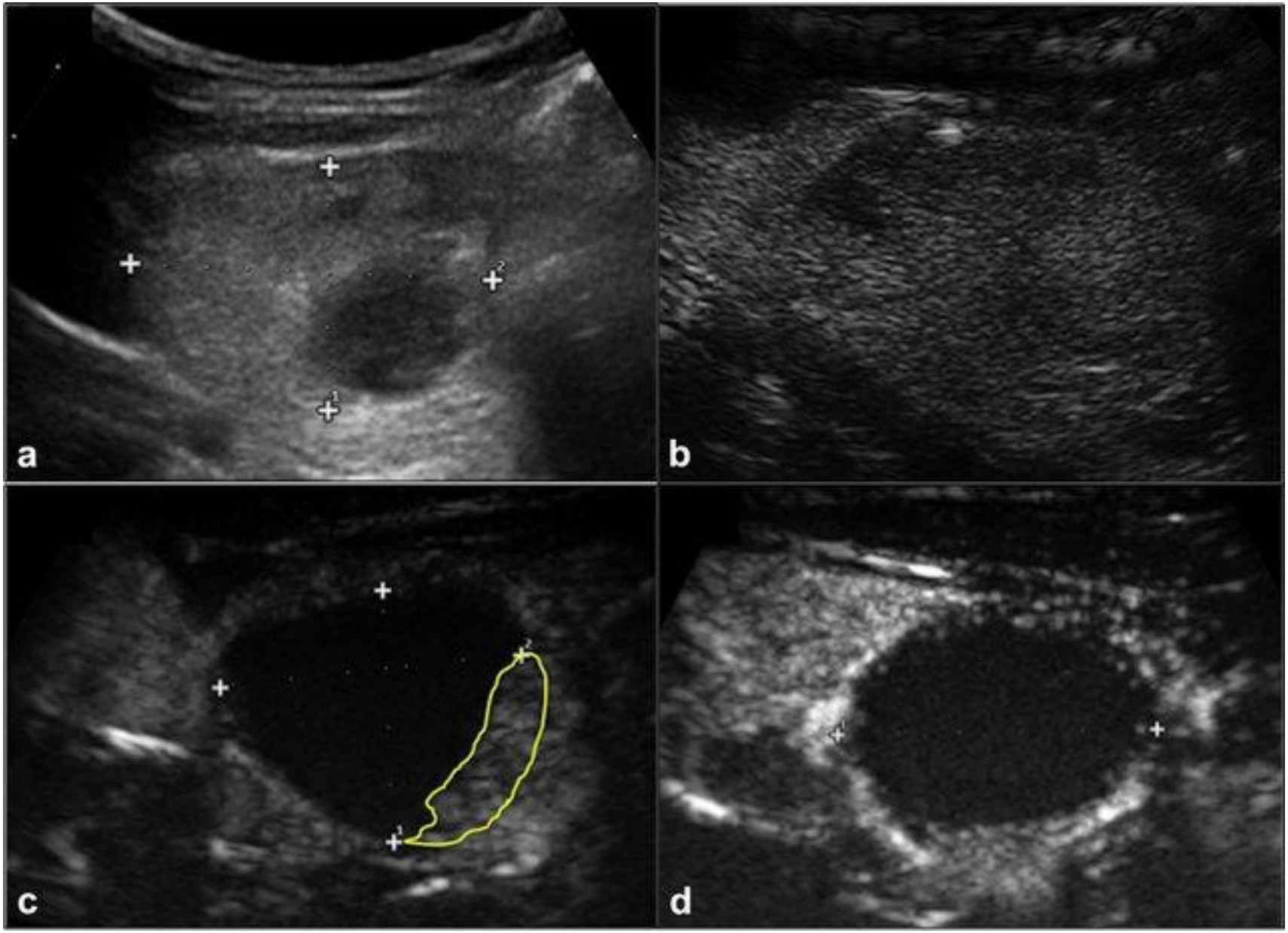
- *Danger triangle, i.e. the tracheoesophageal* groove including the RLN, trachea, and esophagus.

- Ablation should be terminated when all conceptual units have changed to transient hyper echoic zones.

- RFA is usually performed on both the tumor and the surrounding normal tissue in order to prevent local recurrence.


a
b
c
d

- If patients cannot tolerate the pain during ablation, lidocaine injection around the tumour is recommended.

- Based on the clinical framework for risk stratification in determining whether AS is appropriate for PTMC categorized patients as ideal, appropriate, or inappropriate for AS based on imaging findings, and the characteristics of the patient and/or medical team.

- “low-risk” has been described as the absence of clinically evident metastases, local invasion and aggressive cytological evidence.

- Based on strict stratification, the patients classified as inappropriate for AS should not be considered for thermal ablation. However, patients with a fear of undergoing surgery can be considered for thermal ablation.

- However, patients with a fear of undergoing surgery can be considered for thermal ablation.

Treatment efficacy:

- Volume reduction , therapeutic success rate (volume reduction >50%) , complete disappearance of the treated cancer, serum thyroglobulin concentration, cancer perfusion,
- and changes in echogenicity.

Ethanol and thermal ablation for malignant

So Yeong Jeong, Jung Hwan Baek, Young Jun Choi & Jeong Hyun Lee

International Journal of Hyperthermia

2017

The efficacy of RFA:

- The mean reduction in tumour volume ranged from 50.9% to 84%; complete disappearance is noted in 25–94% of cancers ; therapeutic success rates range from 75% to 97% ; symptom improvement is observed in 64% of patients ; and decreases in serum thyroglobulin concentration are noted in most patients.

The efficacy of EA:

- The reduction in the mean cancer volume following EA reportedly ranges from 37.5% to 96%; complete disappearance is noted in31–65% of treated cancers ; therapeutic success rates range from 70.8% to 98% ; and reductions in serum thyroglobulin concentration are noted in some patients.

- RFA is superior to EA because of its better efficacy, fewer mean number of treatment sessions required, and wider extent of the ablation zone. However, RFA demonstrates a higher tendency and severity of voice complications than EA in the treatment of central neck lesions.

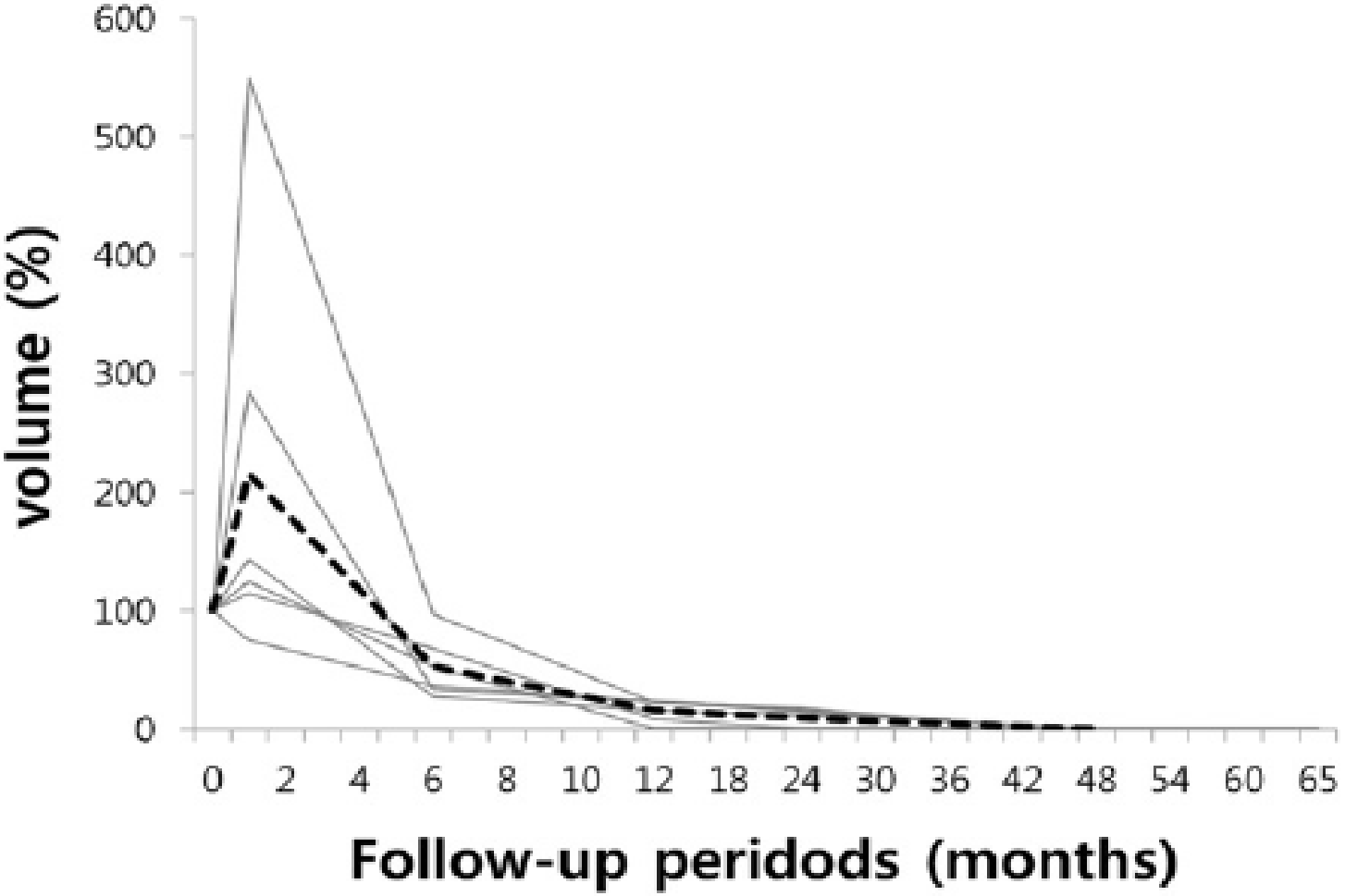


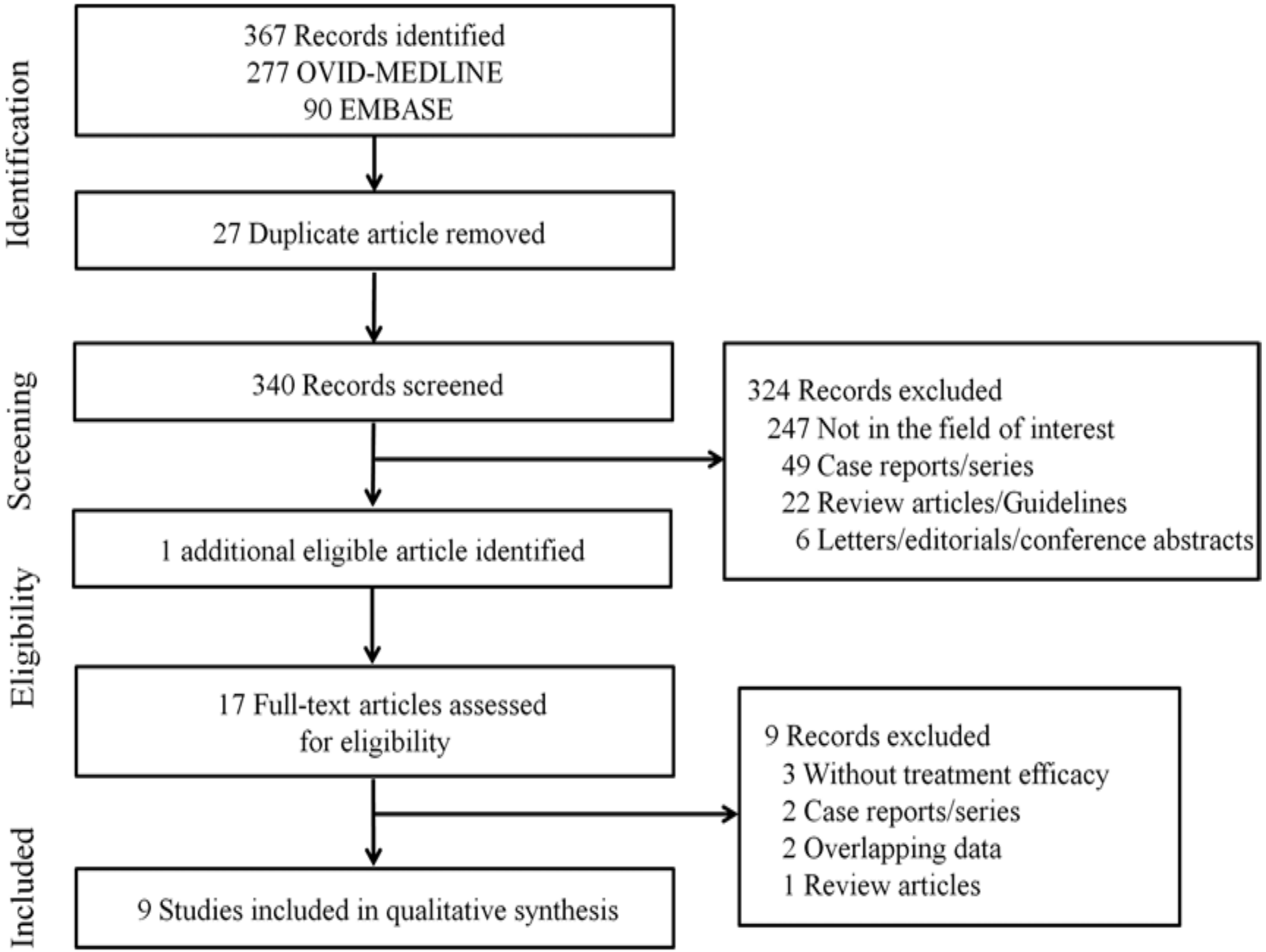
Figure 1. Volume changes of ablation zones after radiofrequency ablation of papillary thyroid carcinomas.

- **Thermal Ablation for Papillary Thyroid Microcarcinomas:**

  Systematic Review and Meta-Analysis:

- THYROID-2019

- 503 low-risk PTMCs in 470 patients treated by thermal ablation from 9 studies.


Identification
Screening
Eligibility
Included
367 Records identified
277 OVID-MEDLINE
90 EMBASE
27 Duplicate article removed
340 Records screened
324 Records excluded
247 Not in the field of interest
49 Case reports/series
22 Review articles/Guidelines
6 Letters/editorials/conference abstracts
1 additional eligible article identified
17 Full-text articles assessed
for eligibility
9 Records excluded
3 Without treatment efficacy
2 Case reports/series
2 Overlapping data
1 Review articles
9 Studies included in qualitative synthesis

Inclusion Criteria:

1- Greatest tumor dimension ≤ 10 mm;

2- Diagnosis by cytology or biopsy,

3-Absence of lymph node (LN) metastasis, distant metastasis, and gross extra thyroidal extension

4-Included evaluation of efficacy after thermal ablation.

- Thermal ablation included MWA, LA, and RFA.

Results of Ablation:

- The mean FU duration after ablation ranged from 7.8 months to over 53 months.

- The mean size of the index tumor before and immediately after ablation and at last FU ranged from 4.3 to 7.5 mm (41 to 157 mm3), 11.8 to 14.1 mm (517.6 to 3099.4 mm3), and 0 to 4mm (0 to 70 mm3), respectively.

- Disappearance rates ranged from 33.7% to 100%.

- Disappearance rate was defined as complete tumor disappearance or the presence of residual scar-like changes.

- None of these patients experienced local tumor recurrence or distant metastasis. However, two patients developed LN metastasis during FU.

  In addition, one patient developed a new cancer, which completely disappeared following additional ablation.

During follow-up, no patient experienced local tumor recurrence or distant metastasis, whereas two patients (0.4%) experienced lymph node metastasis.

One patient (0.2%) developed a new PTMC, which was successfully treated by additional ablation.

Five patients (1.1%) underwent delayed surgery after ablation, including the two patients with lymph node metastasis and three additional patients with unknown etiology.

- The finding, that most of the complications were minor, with transient hoarseness being the most frequent complication, indicates that the operator should be thoroughly trained in US-based anatomy, especially in the evaluation of the *danger triangle*.

- The rate of minor complications per tumor

in the other four studies were 3.4%, 4.3%, 5.4%, and 19%, respectively, with the most common complication being transient hoarseness.

Li J, Liu Y, Liu J, Qian L 2018 Ultrasound-guided percutaneous microwave ablation versus surgery for papillary thyroid microcarcinoma. International journal of hyperthermia : the official journal of European Society for Hyperthermic Oncology, North American Hyperthermia Group **34:653-659.**

Teng D, Sui G, Liu C, Wang Y, Xia Y, Wang H 2018 Long-term efficacy of ultrasoundguided low power microwave ablation for the treatment of primary papillary thyroid microcarcinoma: a 3-year follow-up study. Journal of cancer research and clinical oncology **144:771-779.**

Teng DK, Li HQ, Sui GQ, Lin YQ, Luo Q, Fu P, Du JR, Jin CX, Wang H 2019 Preliminary report of microwave ablation for the primary papillary thyroid microcarcinoma: a large-cohort of 185 patients feasibility study. Endocrine **64:109-117.**

Yue W, Wang S, Yu S, Wang B 2014 Ultrasound-guided percutaneous microwave ablation of solitary T1N0M0 papillary thyroid microcarcinoma: initial experience. International journal of hyperthermia : the official journal of European Society for Hyperthermic Oncology, North American Hyperthermia Group **30:150-157.**

Zhang L, Zhou W, Zhan W, Peng Y, Jiang S, Xu S 2018 Percutaneous Laser Ablation of Unifocal Papillary Thyroid Microcarcinoma: Utility of Conventional Ultrasound and Contrast-Enhanced Ultrasound in Assessing Local Therapeutic Response. World journal of surgery **42:2476-2484.**

- Fatal complications, such as injury to the oesophagus, trachea, or other nerves (i.e. phrenic nerve and brachial plexus), following the treatment of primary or recurrent thyroid cancers, which are often located adjacent to these structures, have not been reported.

- Moreover only 1.1% of patients in the present study underwent delayed surgery after thermal ablation, with none undergoing delayed surgery because of the patient's anxiety about tumor progression. By treating the primary tumor, thermal ablation may alleviate or eliminate patient anxiety.

- Some limitations to this therapy:

- Multifocality was reported to be unilateral or bilateral in 20–40% of patients with PTMC , however, it could not be absolutely excluded without surgical excision.

- LA could not eradicate these occult tumors that are invisible on US, and multifocality is also significantly associated with lymph node metastasis and disease recurrence in PTMC.

- Because the ablation procedure is totally operator dependent, the qualities of the operator and the treatment center are essential.

- The operator needs to being fully competent with the technical aspects of thermal ablation, including the use of a small active tip, the moving shot technique, and hydro-dissection, thereby maximizing the efficacy and minimizing complications associated with thermal ablation.

- The operator should be thoroughly trained in US-based anatomy, especially in the evaluation of the *danger triangle, i.e. the tracheoesophageal* groove including the RLN, trachea, and esophagus.

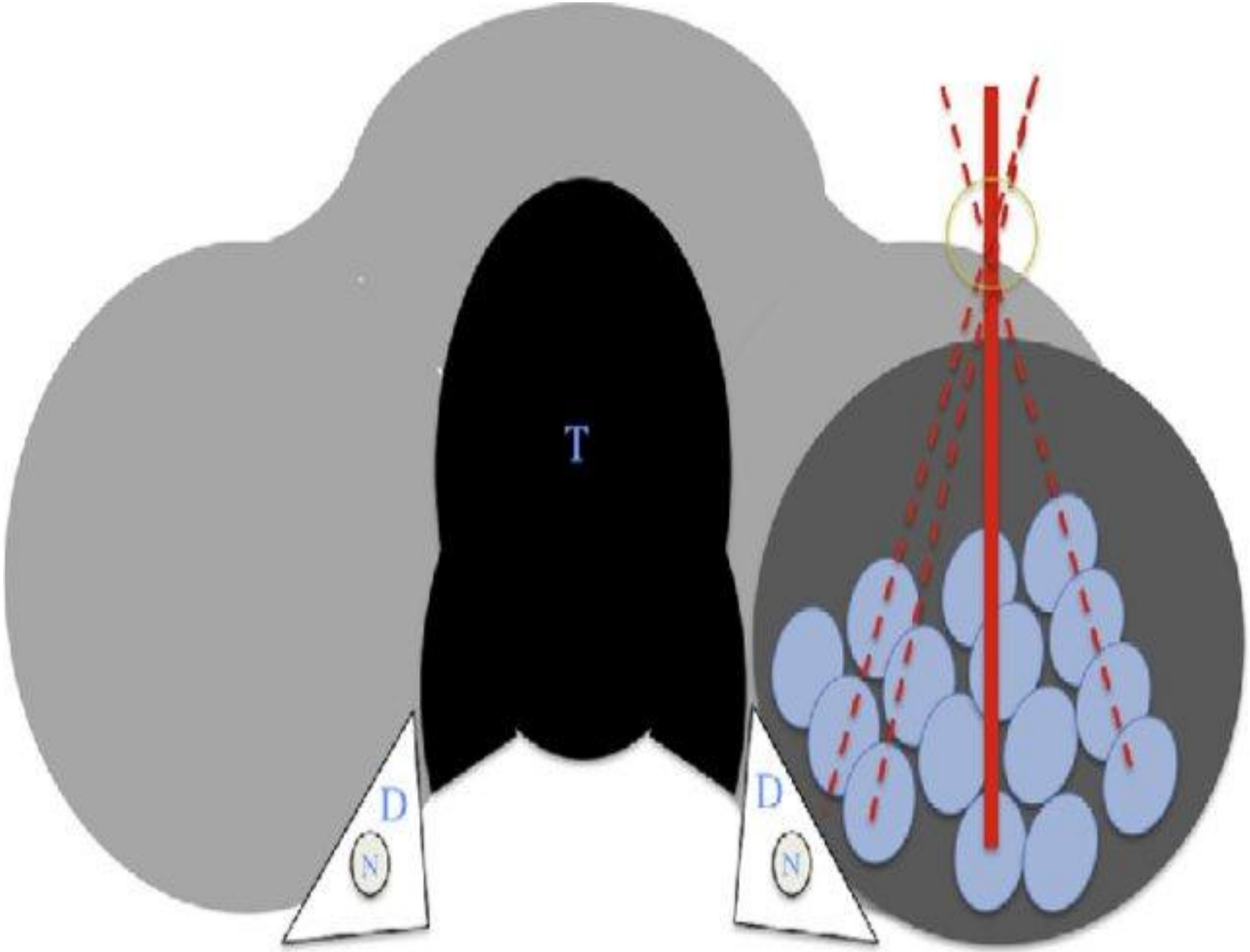
- In the LA group, there was no guarantee that all patients had no central lymph node metastasis. Therefore, the decision to perform LA instead of surgery to treat PTMC should be made cautiously.

Pathologically confirmed PTC without cytological aggressiveness,

Single PTC without extra thyroidal extension

No metastatic tumors at the time of treatment,

Recently, papillary thyroid carcinoma variants detected via US have been reported .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Aggressive	Less favorable	Favorable
Tall cell variant	Solid variant	Follicular (encapsulated) variant
Columnar cell variant	Diffuse sclerosing variant	Cribriform-morular variant
Hobnail variant		Warthin-like variant

Tall Cell Variant

On ultrasonography, TCV tumors often appear as microlobulated, markedly hypoechoic nodules with microcalcifications and extrathyroidal extension, and are always associated with lymph node metastasis.

Columnar Cell Variant

On US, encapsulated tumors appear as

circumscribed hypoechoic nodules with or without microcalcifications and aggressive tumors as large microlobulated hypoechoic nodules, often with capsular protrusions representing extrathyroidal extension and neck nodal metastasis.

Hobnail Variant

This variant has been found to show a palpable mass appearing as a microlobulated hypoechoic nodule with microcalcifications and multiple metastatic lymph nodes on US.

Variant	Incidence	Common ultrasonographic feature
Tall cell variant	4%–17% of PTCs	Typical malignant features[a], frequent nodal metastasis
Columnar cell variant	No report	Typical malignant features vs. circumscribed border
Hobnail variant	No report	Typical malignant features, frequent nodal metastasis
Solid variant	3% of PTCs	Typical malignant features vs. circumscribed border
Diffuse sclerosing variant	0.7%–6.6% of PTCs	Ill-defined mass, scattered microcalcifications, nodal metastasis
Follicular variant (encapsulated)	10%–20% of all thyroid cancers	Solid hypoechoic or isoechoic nodule
Cribriform-morular variant	1% of FAP patients	Solid oval to round nodule without calcification
Warthin-like variant	No report	Benign-looking nodule, heterogeneous parenchyma

Group	Source, publication	Study period	Institution	Patient No.	Mean age	Male: female	Study Design	Tumor No.	Criteria for ablation (summery of inclusion and exclusion criteria)
LA	Zhang et al, 2018 (15)	November 2013 – July 2016	Rui Jin Hospital, China	64	42.5	23:41	Retro.	64	(1) single PTMC by cytology; (2) no LN or distant metastasis; (3) no contact or disruption of the thyroid capsule (4) no isthmic lesion; (5) no massive calcification (>2 mm), (6) no type of thyroid malignancy; (7) solid without cystic components; (9) unsuitable for or unwilling to undergo surgery

- In conclusion that thermal ablation methods are safe and effective for local tumor control in patients with low-risk PTMCs, minimizing the delayed surgery rate.

- Strict inclusion criteria and technical proficiency are required to maximize favorable results.

- Among them, aggressive variants should be carefully evaluated before ablation. Furthermore, the operator should carefully evaluate thyroid capsule invasion or lymph node metastasis.