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Progress in research on ablation of thyroid nodules

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Abstract

The incidence of thyroid nodules is rising annually. Surgical treatment is effective, but often results in significant trauma, recurrent laryngeal nerve injury, hypoparathyroidism, and other complications. Recent years have seen significant breakthroughs in thyroid nodule ablation for treating thyroid diseases, although its application remains controversial.

The objective was to review the development history and current research status of thyroid nodule ablation to provide a reference for future studies.

The literature on thyroid nodule ablation was reviewed, analysing its advantages and disadvantages.

The therapeutic effect of thyroid nodule ablation in treating benign thyroid lesions is noteworthy, but issues such as lax treatment indications and excessive medical treatment persist. Initial success has been achieved in treating thyroid malignant lesions, particularly papillary thyroid microcarcinoma (PTMC). However, the curative effect requires further follow-up verification. **(Endokrynol Pol 2024; 75 (3): 262–266)**

Key words: *thyroid nodules; ablation; PTMC; MDT; operation*

Introduction

As people's living standards improve, along with an increased willingness for physical examinations and the use of more sophisticated imaging equipment, the detection rate of thyroid nodules has been increasing annually [1]. Consequently, its related mortality rate has also shown an upward trend [2, 3].

Thyroid nodules typically appear in young to middle-aged women. The primary clinical symptom of benign nodules is a painless neck mass, which can cause discomfort when swallowing and shortness of breath after compressing the oesophagus and trachea. Malignant nodules are typically found during physical examinations, with occasional large ones found during initial diagnoses in outpatient departments. Currently, the primary treatment methods for thyroid nodules are medication and surgery. Surgical treatment is comprehensive, but it carries risks such as visible surgical scars, recurrent laryngeal nerve injury, and parathyroid gland injury. These risks perplex many clinicians and impact patients' quality of life. Ablation treatment provides a new solution for it [4, 5].

Ablation therapy summary

Ablation therapy is a treatment method that directly targets specific focal lesions (single or multiple), guided by images, to eradicate or destroy pathological tissues. The primary ablation treatment methods include chemical ablation (ethanol ablation, acetic acid, etc.) and physical ablation [freezing, laser, high intensity focused ultrasound, radiofrequency (RFA), microwave (MWA), hot distilled water, etc.].

Chemical ablation

Chemical ablation methods commonly used include absolute ethanol and acetic acid injections. Anhydrous ethanol ablation is the most commonly used method of chemical ablation in clinics. Anhydrous ethanol, due to its strong hydrophilicity, can cause dehydration of the cell membrane, cytoplasm, and organelle, leading to protein denaturation and cell death upon contact with cells. Simultaneously, it can induce thrombosis in the microcirculation of nodules and surrounding tissues with damaged vascular endothelial cells, leading to ischaemia and hypoxia, and indirectly causing necrosis of diseased tissues.

In clinical procedures, ablation doctors frequently inject 75% absolute ethanol mixed with a small quantity of lidocaine into lesions, guided by computed tomography (CT) or B-ultrasound. Lidocaine is used to alleviate patient pain and discomfort.

Acetic acid ablation commonly uses 50% acetic acid. Acetic acid has higher permeability and a stronger

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therapeutic effect than absolute ethanol, but its treatment causes significant patient discomfort, and it has a more pungent smell.

Chemical ablation is simple and quick, but its therapeutic effect is unstable, often necessitating repeated treatment, particularly for nodules larger than 3 cm and some mixed nodules. Conversely, physical ablation can achieve superior therapeutic effects using heat energy.

Physical ablation

Common physical ablation methods include freezing, laser, high-intensity focused ultrasound, radio frequency, microwave, and hot distilled water, among others. Apart from cryoablation, the other 5 ablation methods can also be termed as thermal ablation.

Cryoablation uses a special needle core to transport refrigerant, enabling the diseased tissue to swiftly cool to target temperature 1, then rapidly return to target temperature 2. Repeating the freeze-rewarm process twice can cause diseased cells in the target area to rupture and sustain damage. Additionally, the microvascular intima may also be damaged and embolised, thereby reversing the tumour's immunosuppressive state. Cryoablation offers benefits such as minimal bleeding, mild pain response, and a broad scope of action, but it requires a lengthy ablation time. Additionally, large argon and helium pressure tanks are necessary.

The principle of thermal ablation states that immediate coagulation necrosis occurs in human tissues when the temperature is between 60 and 100 , and tissues rapidly carbonise and gasify when the temperature exceeds 105 . Radiofrequency ablation uses alternating current resistance to generate heat, while microwave ablation uses a 1–2-GHz electromagnetic wave to oscillate polar molecules for heat generation. Laser ablation employs a 1064 monochrome laser to produce heat. High-intensity focused ultrasound converges low-energy, low-intensity ultrasonic beams into a high-intensity, high-energy focus in the direction of ultrasonic propagation. Lastly, hot distilled water ablation uses its heat energy and low permeability characteristics to eliminate diseased tissues.

Application of ablation technology in benign thyroid nodules

Historically, surgeons operated on large, symptomatic benign thyroid nodules in medical practice. Additionally, some patients with cosmetic requirements opted for endoscopic thyroid surgery via various methods. Since the late 1990s, some scholars have begun exploring the application of ablation technology in animal and human tissues. Over the past 20 years, societies worldwide have recognised the ablation effect of benign nodules [1, 6, 7].

Ethanol ablation is suitable for treating involuntary functional nodules, specifically cystic nodules [8]. For recurrent cystic nodules or cystic solid nodules, radiofrequency or microwave ablation is appropriate.

Thyroid nodule volume can be significantly reduced by ablation treatment. Luo et al. administered microwave ablation treatment to 180 thyroid nodules. After a 3-year follow-up, it was observed that the nodule volume reduction rate within 12 months post-ablation was related to the nodule's nature, with cystic nodules showing a higher reduction rate. However, no clear relationship was found between the volume reduction rate and the nodule's nature during the 12–36-month follow-up period. The total nodule volume decreased by over 90% during the 36-month follow-up [9].

Ablation therapy has a minimal effect on normal thyroid function. A study retrospectively analysed data from 48 patients with benign thyroid nodules larger than 4 cm who received microwave ablation (MWA) and 53 patients who underwent lobectomy. It found that the volume reduction rate in the MWA group was approximately 85–95%. Additionally, the operation time, incision length, and hospitalisation time were shorter in the MWA group, and complications and thyroid function changes were less significant [10]. Similar conclusions have been reached by other studies comparing thermal ablation with conventional open surgery and endoscopic surgery for thyroid nodules [11–13].

Ablation also positively impacts autonomous functional nodules. An Italian multicentre retrospective study demonstrated that, during a 3-year follow-up period, the volume of autonomic nodules significantly decreased and serum TSH levels significantly increased post thermal ablation treatment. The treatment effect was more pronounced for smaller nodus [14].

Different ablation methods for thyroid nodules may have varying long-term effects. A meta-analysis by Guo et al. revealed that radiofrequency ablation and microwave ablation exhibit equal safety and effectiveness in benign nodule ablation. However, the volume reduction rate one year after radiofrequency ablation surpasses that of microwave ablation [15].

Application status of ablation technology in malignant thyroid nodules

In recent years, scholars have extensively explored the ablation of thyroid malignant nodules. Aside from some unresectable thyroid malignant tumours, the primary research focus is on papillary thyroid micro carcinoma (PTMC). PTMC is a benign, inert tumour.

Current treatment methods include dynamic monitoring, ablation, and surgical treatment [16, 17].

Yan et al. conducted a retrospective analysis of 884 patients with thyroid micropapillary carcinoma who underwent either lobectomy or radiofrequency ablation. They found no significant difference in the curative effects of radiofrequency ablation and lobectomy. However, patients treated with radiofrequency ablation had shorter hospital stays and lower costs [18]. A retrospective analysis of data from thyroid isthmus nodules treated by ablation or total thyroid lobectomy showed that the 2 treatments were equivalent [19]. A Korean research team reported the 10-year follow-up results of 90 PTMC patients who underwent laser ablation. Of these, 84 patients remained stable during the follow-up, with no new or metastatic lesions appearing [20]. The safety and effectiveness of laser ablation in patients with multifocal PTMC have been confirmed as well [21]. A 5-year follow-up study demonstrated that radiofrequency ablation has the same therapeutic effect as unilateral lobectomy plus prophylactic neck lymph node dissection for patients with unilateral multifocal PTMC. There was no significant difference in recurrence and metastasis rate [22]. There was no difference in recurrence rates between microwave ablation and surgery for T1N1M0 PTMC [23]. Microwave ablation for low-risk multifocal PTMC has also achieved gratifying results [24].

A meta-analysis of 13 non-randomised controlled studies demonstrated a volume reduction rate of 98.91% [95% confidence interval (CI)] following papillary thyroid carcinoma (PTC) thermal ablation treatment. The complete tumour disappearance rate was 83% (95% CI: 97.98–99.83%), the new tumour rate was 0.3%, the lymph node metastasis rate was 0.0%, and the range was 67–94%. The study also found that the rate of complete tumour disappearance over 3 years was significantly higher in patients treated with RFA than in those treated with MWA [25]. Researchers have systematically evaluated the efficacy of RFA on low-risk PTMC, concluding that RFA is safe and feasible for treating low-risk PTMC [26].

Compared to dynamically observed PTMC patients, those treated with thermal ablation experience less anxiety, making it less likely for them to opt for surgery to remove thyroid nodules due to anxiety [27].

Advantages and disadvantages of ablation in the treatment of thyroid nodules

The primary benefits of ablation in treating thyroid nodules include the following: 1. no hospitalisation required, or the duration of hospitalisation is significantly reduced [28]; 2. the treatment effect of cystic nodules is immediate; 3. for elderly patients, the risk of surgery can be effectively avoided; 4. compared with surgery, it has little effect on thyroid function; and 5. there is no scar from neck surgery, and the patient has a good medical experience [29].

However, the following problems also exist with thyroid nodule ablation: 1. some benign nodules frequently recur and require multiple ablation treatments; 2. most benign nodules that are asymptomatic can be observed and not treated for now. Premature intervention might lead to wasted medical resources and heightened economic and psychological burdens for patients; and 3. currently, there are few guides for the ablation treatment of malignant nodules, leading to irregular diagnosis and treatment.

Complications and management measures after thyroid ablation

The complication rate of thyroid nodule ablation is less than 5% [11, 14, 22, 30]. Postoperative complications include neck pain, neck haemorrhage, neck haematoma formation, skin burns, hypothyroidism, nausea, vomiting, tracheal injury, nerve injury (manifested as hoarseness, drinking cough, Horner syndrome), tumour rupture, iatrogenic tumour metastasis, and incomplete ablation of malignant tumour [6, 31, 32]. Additionally, instances of jugular vein thrombosis have been reported after thyroid ablation [33].

If necessary, neck pain after ablation can be treated with oral analgesic drugs, mainly non-steroidal antiinflammatory drugs (NSAIDs). Neck haemorrhage and haematoma often self-absorb after ablation; thus, routine compression is recommended post ablation. Accidental skin burns can cause anxiety in patients and impact the effectiveness of ablation treatment. If necessary, please consult a plastic surgery doctor for treatment assistance. Postoperative nausea and vomiting are rare. If necessary, certain antiemetic and acid-inhibiting stomach-protecting drugs can be used for relief.

Inaccurate preoperative evaluation and operator inexperience often cause tracheal and nerve injuries after ablation. Scholars retrospectively analysed 368 single PTC patients treated with thermal ablation. They found that post-ablation hoarseness was related to the T stage, the distance between nodules and the anterior, medial, and posterior thyroid capsule, the distance from the tracheoesophageal groove, and whether medial isolation fluid was injected [25]. To mitigate nerve damage caused by thermal injury, timely application of a special coolant to the injured nerve is recommended. Surgical treatment is required for tracheal injury when necessary. If a nodule ruptures during surgery, ensure proper drainage and use antibiotics to prevent infection if needed.

Tumour metastasis from ablation needles, rarely reported, aligns with the principle of tumour metastasis from thyroid fine needle punctures. It is suggested that operations be standardised to minimise their occurrence as much as possible.

Incomplete malignant tumour ablation is common in large tumour nodules, or those close to the thyroid dorsal membrane, trachea, oesophagus, and important blood vessels, especially when the tumour is not carefully classified before the operation. The recurrence of malignant nodules after ablation may also be related to insufficient preoperative evaluation [19, 20]. Therefore, standardised diagnosis and treatment are imminent. Before operation, a puncture must be performed, the malignancy of nodules should be graded, and the presence of intraglandular or distant lymph node metastasis should be accurately evaluated. Concurrently, a preoperative notification should be issued, enabling patients to gain detailed knowledge about thyroid ablation treatment [6, 7].

Follow-up suggestions after thyroid ablation

For patients without major complications, nodule size should be evaluated 1 month, 6 months, and 12 months post operation, and every 6 months thereafter. It is recommended that the follow-up interval be shortened for patients with major complications. The follow-up evaluation primarily includes checking for discomfort symptoms, changes in ultrasonic nodule size, thyroid function tests, and endoscopic examinations of the trachea and vocal cords [6, 7].

Conclusion

Thyroid nodule ablation, a new treatment method, has a reliable effect, causes less trauma, minimally influences thyroid function, and results in mild complications in the treatment of thyroid micropapillary carcinoma. Current preliminary research results affirm the curative effect of treatments for thyroid micropapillary carcinoma. However, doctors often deviate from consensus in their diagnostic and treatment practices [34]. Ablation, used excessively in the diagnosis [34] and treatment of thyroid nodules, can lead to premature intervention of smaller nodules and lax indication during treatment. This increases the incidence of complications, particularly for some PTMC patients, who lack accurate pathological evaluation. Considering this, there is an urgent need for new guidelines to standardise and guide thyroid ablation treatment. Before the ablation treatment of suspected malignant nodules identified through imaging examination, a multidisciplinary discussion group — comprising the imaging, thyroid surgery, endocrinology, pathology, and radiotherapy departments — should collaboratively discuss and formulate a diagnosis and treatment plan. Only through down-to-earth and standardised diagnosis and treatment can thyroid ablation technology develop rapidly and healthily, better serve patients, and improve the quality of diagnosis and treatment.

Author contributions

Z.Y., L.-B.M. designed the experiment. Z.Y., X.-H.P., H.-T.H., L.-B.M. collected and organized the literature, and Z.Y., X.-H.P., L.-B.M. wrote the manuscript.

Data availability

No underlying data was collected or produced in this study.

Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this article

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REVIEW

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