

# Traditional Chinese Medicine Treatment of Thyroid Cancer: A Review

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**Abstract:** Thyroid cancer is the most common malignancy of the endocrine system, and its incidence has been increasing in recent years. Traditional Chinese Medicine (TCM) has shown unique advantages in supporting the treatment and management of thyroid cancer. This review provides a comprehensive overview of current literature on TCM-related interventions for thyroid cancer, covering theoretical foundations, epidemiological features, pathophysiological mechanisms, diagnostic applications, clinical practices, technological progress, and existing challenges to summarize the clinical effectiveness of TCM, clarify its role in integrated treatment strategies, and outline future directions for research and clinical application.

**Keywords:** thyroid cancer, PTC, WDTC, ATC, TMC

## Introduction

Thyroid cancer is a malignancy arising from either follicular epithelial or parafollicular C cells of the thyroid gland. Among tumors originating from follicular cells, four distinct histological subtypes have been identified: papillary thyroid cancer (PTC), follicular thyroid cancer (FTC), poorly differentiated thyroid cancer (PDTC), and anaplastic thyroid cancer (ATC).<sup>1</sup> Of these, PTC and FTC are collectively referred to as well-differentiated thyroid cancers (WDTC), accounting for most cases.<sup>2</sup>

Surgical resection remains the cornerstone of treatment for most patients with thyroid cancer.<sup>3</sup> In cases classified as low-risk WDTC, surgery alone is often sufficient, while those with high-risk features typically require adjunctive therapies such as thyroid-stimulating hormone (TSH) suppression and radioiodine therapy (RAI).<sup>4</sup> Despite the recognized aggressiveness of ATC, a substantial proportion of thyroid cancer-related mortality stems from the progression of RAI-refractory WDTC. The limited efficacy of current therapeutic options for advanced-stage disease highlights the need for alternative or complementary strategies to improve outcomes.

Traditional Chinese Medicine (TCM), a long-standing component of Chinese healthcare, has gained increasing interest for its potential application in cancer treatment, including thyroid cancer.<sup>5</sup> TCM is based on unique theoretical principles that view disease as a result of imbalances in the flow of qi (vital energy) and dysfunction of the internal organs, collectively referred to as the zang-fu system.<sup>6</sup> These organs are considered functional units responsible for regulating physiological processes. In the context of thyroid cancer, TCM theory suggests that dysfunctions in the liver, spleen, and kidney may lead to stagnation of qi, accumulation of phlegm, and the generation of internal heat, which together promote tumor formation.<sup>7</sup> TCM treatment emphasizes syndrome differentiation and a holistic approach, aiming to rebalance organ function, regulate immune activity, and inhibit tumor progression through personalized therapeutic strategies.<sup>8</sup>

Emerging clinical and experimental evidence has highlighted the adjunctive value of TCM in alleviating symptoms, reducing recurrence, and improving quality of life in patients with thyroid cancer.<sup>9</sup> Given these observations, this review aims to systematically summarize the theoretical foundations, therapeutic strategies, clinical applications, and recent advancements related to the use of TCM in the integrative management of thyroid cancer. Through this comprehensive

analysis, the study seeks to elucidate the potential of TCM to complement conventional treatments and contribute to improved clinical outcomes in thyroid cancer care.

## Basic Pathophysiology of Thyroid Cancer

### Cellular, Genetic, and Molecular Features of Thyroid Cancer

The development and progression of thyroid cancer involve a complex interplay of cellular, genetic, and molecular factors. Thyroid cancer cell lines have long served as important *in vitro* models for investigating tumor biology and identifying therapeutic targets.<sup>10</sup> However, limited representation in established panels such as the NCI-60 and inconsistencies in cell line classification have hindered progress in this area. Recent efforts have identified 23 cell lines with confirmed or probable thyroid origin, offering improved models for studying disease mechanisms.<sup>11</sup>

A key cellular feature of thyroid cancer is the presence of cancer stem-like cells (CSCs), which possess self-renewal and differentiation capabilities and are associated with increased tumorigenicity, metastatic potential, and resistance to chemoradiotherapy.<sup>12</sup> These CSCs are present across major thyroid cancer subtypes and can be identified by markers such as CD133, CD44, and aldehyde dehydrogenase. Additionally, epithelial-mesenchymal transition (EMT) contributes to tumor aggressiveness, and analysis of EMT-related markers has helped elucidate mechanisms of invasion and metastasis.<sup>13</sup>

Genetically, thyroid cancer is marked by both inherited and somatic alterations. In familial medullary thyroid cancer (MTC), mutations in the RET proto-oncogene are commonly observed, while familial non-medullary thyroid cancer may involve autosomal dominant mutations with variable penetrance.<sup>14</sup> Several susceptibility genes, including HAP2, DUOX2, and WDR77, have been identified in hereditary and sporadic cases.<sup>14–16</sup> Subtype-specific mutations such as BRAF, RAS, RET/PTC rearrangements (in PTC), and PAX8/PPAR $\gamma$  fusions (in FTC) play critical roles in defining histological subtypes and guiding treatment strategies.<sup>17</sup> Polymorphisms in DNA repair genes, such as XRCC3 rs861539 and XPC rs2228001, may further influence cancer risk.<sup>18</sup>

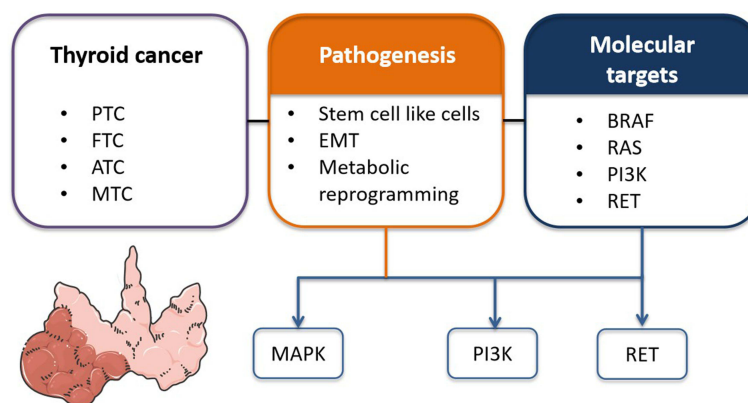
These genetic alterations converge on several key molecular signaling pathways. The MAPK and PI3K pathways are central to thyroid carcinogenesis, regulating processes including proliferation, differentiation, and apoptosis.<sup>19–21</sup> Activating mutations in BRAF and RAS promote MAPK pathway activation, while PI3K pathway alterations are more commonly associated with follicular and aggressive tumor phenotypes.<sup>22</sup> Germline variants affecting MAPK/ERK and PI3K/AKT pathways have also been observed in familial thyroid cancer cases.<sup>23–25</sup> Furthermore, proteins such as MUC15 have been shown to promote tumor progression by modulating signaling through GPCR/ERK and integrin-FAK pathways, also enhancing CSC characteristics.<sup>26</sup> Therefore, understanding these interconnected pathways provides a foundation for the development of targeted therapeutic approaches in thyroid cancer.

### Effect of TCM on the Pathological Mechanism of Thyroid Cancer

Emerging research suggests that TCM may modulate the pathological mechanisms of thyroid cancer by targeting various aspects of the tumor microenvironment (TME), immune response, and metabolic pathways. The TME, comprising cancer cells, immune cells, fibroblasts, and extracellular matrix, plays a critical role in tumor proliferation, invasion, immune evasion, and therapeutic resistance. A representation of the pathophysiology of thyroid cancer is shown in [Figure 1](#).

Several active compounds derived from Chinese herbal medicine have demonstrated antitumor effects through immune modulation. For instance, ginsenoside Rg3, a bioactive component of *Panax ginseng*, has been shown to significantly inhibit the migration and invasion of papillary thyroid cancer (PTC) cells (TPC-1, BCPAP, C643, and Ocut-2c) and reduce pulmonary metastasis in murine models. Mechanistically, Rg3 disrupts actin cytoskeletal organization by downregulating Rho GTPases (Rac-1 and Cdc42), thereby impairing lamellipodia formation. It also suppresses key regulators of metastasis, including MMP-2, MMP-9, VEGF-C, and VEGF-A, and reduces CD31 expression in both PTC and anaplastic thyroid cancer (ATC) tissues, suggesting inhibition of both lymphatic and angiogenic pathways.<sup>27</sup> These findings highlight Rg3's potential as an anti-metastatic agent for advanced thyroid cancer.

In addition to influencing the immune microenvironment, TCM can modulate metabolic reprogramming in tumor cells. Tumor cells frequently adopt aerobic glycolysis (the Warburg effect) to support rapid proliferation. Natural products such as apigenin, genistein, and curcumin have been shown to inhibit glycolysis and related signaling pathways



**Figure 1** Schematic representation of the pathophysiological mechanisms involved in thyroid cancer.

in thyroid cancer, leading to reduced glucose uptake and lactate production, thereby limiting the metabolic flexibility of cancer cells.<sup>28</sup> These compounds also affect key signaling cascades such as PI3K/Akt/mTOR, MAPK/ERK, and JNK/p38, which regulate tumor growth, apoptosis, and inflammatory responses.

Furthermore, recent network pharmacology and *in vivo* experimental studies of *Scrophulariae Radix* (Xuanshen, XS) have demonstrated its multifaceted therapeutic effects in thyroid hormone-related disorders. XS exerts antioxidant, anti-inflammatory, and anti-apoptotic effects by modulating Bcl-2, BAD, ERK1/2, JNK, and p38 pathways, and by decreasing TNF- $\alpha$ , IL-1 $\beta$ , and IL-6 expression in liver and kidney tissues. In mice treated with levothyroxine-induced hyperthyroidism, XS not only restored thyroid hormone levels but also preserved liver and kidney function, indicating systemic protective effects relevant to thyroid hormone dysregulation.<sup>29</sup>

Taken together, these studies suggest that TCM may act on multiple pathological mechanisms in thyroid cancer, including immune regulation, inhibition of metastatic signaling, suppression of aberrant metabolism, and systemic protection against thyroid hormone-related damage. These findings provide a scientific basis for clinical trials on TCM in integrative treatment approaches and highlight its potential for future translational research.

## Epidemiological Analysis of Thyroid Cancer

### Global Incidence and Mortality of Thyroid Cancer

The global incidence of thyroid cancer is increasing and the mortality rate remains relatively stable or declines. According to GLOBOCAN 2022, there are approximately 821,214 new cases and 47,507 deaths attributed to thyroid cancer worldwide, with a higher incidence in women than in men.<sup>30</sup> Variations in morbidity and mortality rates are evident across different countries and regions; specifically, nations with a high Human Development Index (HDI) exhibit incidence rates approximately ten times greater than those in countries with a low HDI, while mortality rates tend to be more consistent across various regions.

Regionally, China represents a significant portion of the global burden of thyroid cancer, accounting for 56.77% of total cases and 24.35% of related deaths worldwide, with the highest incidence reported in men.<sup>30</sup> Furthermore, there has been an increase in the incidence of thyroid cancer among children and adolescents, with girls exhibiting a higher incidence than boys. However, the mortality rate in this demographic remains low, with the age-standardized mortality rate falling below 0.1/million in all countries.<sup>31</sup>

### Risk Factors and Prevalence of Thyroid Cancer

Numerous risk factors have been identified in relation to thyroid cancer. Autoimmune thyroid diseases, particularly those characterized by elevated serum levels of thyroglobulin antibodies (TgAb), have been linked to an increased risk of developing thyroid cancer.<sup>32</sup> Obesity is recognized as a potential risk factor, with a concurrent increase in the prevalence of both obesity and thyroid cancer. However, the influence of obesity on the aggressiveness of thyroid cancer and its response to treatment remains debatable.<sup>33</sup>

Furthermore, dietary habits may play a significant role in modulating the risk of thyroid cancer. Research indicates that patients with differentiated thyroid cancer exhibit a markedly lower intake of vegetables, fruits, saltwater fish, and low-fat cheese than a control group, while their consumption of starchy foods, particularly white bread, is higher. This suggests that a diet abundant in vegetables, fruits, and saltwater may serve as a protective factor against thyroid cancer.<sup>34</sup> Genetic predispositions are crucial in the etiology of thyroid cancer, with a family history of the disease being a well-established risk factor.<sup>35</sup>

## Early Screening and Preventive Strategies for Thyroid Cancer

The efficacy of early screening strategies for thyroid cancer remains debatable. The United States Preventive Services Task Force advises against routine screening for thyroid cancer in asymptomatic adults, positing that the potential harm of screening surpasses its benefits.<sup>36</sup> Nevertheless, screening may be warranted for individuals with specific risk factors, including those with a history of childhood exposure to ionizing radiation, hereditary thyroid cancer syndromes, or familial history of thyroid cancer.<sup>37</sup>

Ultrasound is recognized as a primary diagnostic tool for thyroid disease in screening methodologies; however, its high sensitivity may result in overdiagnosis of many indolent thyroid cancers.<sup>38</sup> Research involving the screening of relatives of patients with familial non-medullary thyroid cancer (FNMTC) indicates that thyroid ultrasound can facilitate earlier detection of thyroid cancer, with findings suggesting that patients identified through screening tend to be younger and exhibit a lower incidence of extrathyroidal invasion.<sup>39</sup> Nonetheless, the potential for overtreatment associated with screening necessitates thorough evaluation of the associated risks and benefits, thereby underscoring the importance of developing personalized screening strategies.

## Advances in the Diagnosis of Thyroid Cancer

### Imaging Diagnostic Techniques of Thyroid Cancer

Accurate diagnosis is an essential step in the effective management of thyroid cancer and provides the foundation for selecting appropriate treatment strategies, including the integration of TCM. Imaging modalities not only assist in the initial detection and characterization of thyroid nodules but also play an important role in monitoring disease progression and evaluating treatment response. In clinical practice, ultrasound remains the first-line imaging modality due to its high sensitivity in detecting thyroid nodules and assessing cervical lymph nodes, but despite its widespread use, conventional B-mode ultrasound has limited specificity, making it difficult to confidently differentiate benign from malignant nodules and often resulting in unnecessary invasive procedures such as fine-needle aspiration (FNA) or surgery.<sup>38</sup>

To improve diagnostic precision, multimodal ultrasound techniques have been developed, combining B-mode imaging with elastography and contrast-enhanced ultrasound. This integrated approach allows for a more comprehensive evaluation of nodule morphology, vascularity, and tissue stiffness, which are key parameters in risk stratification. Recent studies have shown that such multimodal imaging significantly improves diagnostic accuracy, reaching an area under the curve (AUC) of 0.985, compared to 0.841 for B-mode alone.<sup>40</sup> These advancements are particularly valuable in the context of integrative treatment planning, where precise diagnosis supports the selection of individualized TCM interventions based on tumor characteristics.

Beyond anatomical assessment, functional imaging techniques provide additional diagnostic value. Nuclear medicine imaging, particularly with radioiodine isotopes such as I-123 or I-131, is frequently used to evaluate thyroid function and to detect residual or metastatic lesions in patients with differentiated thyroid cancer. This modality is especially relevant following surgical resection, aiding in postoperative surveillance and guiding decisions regarding radioiodine therapy. In cases where tumors lose iodine avidity, 18F-fluorodeoxyglucose positron emission tomography (FDG-PET) becomes a valuable tool, offering insight into the metabolic activity of the tumor and improving the detection of recurrent or aggressive disease.<sup>41,42</sup> Such information is not only vital for staging and prognosis but also for determining when patients may benefit from adjunctive TCM-based therapies aimed at supporting immune function or alleviating systemic symptoms.

In addition to established methods, novel optical imaging technologies are being investigated for their potential role in thyroid cancer diagnosis and treatment. These techniques, which utilize the optical properties of tissues such as light

absorption, refraction, and scattering, may enable high-resolution, real-time visualization of tumors with minimal invasiveness. Although still in the research phase, optical imaging holds promise for both diagnostic and intraoperative applications, including the delineation of tumor margins during surgery. From a TCM perspective, these innovations may complement traditional diagnostic approaches such as inspection and palpation, offering an opportunity for integrative diagnostic models that combine ancient practices with modern technologies.<sup>43</sup>

In summary, the ongoing advancement of imaging techniques enhances the precision and depth of thyroid cancer diagnosis, facilitating tailored treatment approaches that include both Western medical procedures and Traditional Chinese Medicine. By improving the ability to detect, characterize, and monitor thyroid malignancies, these diagnostic tools form an essential bridge between modern oncologic assessment and TCM-based therapeutic decision-making.

## Pathological Diagnostic Criteria of Thyroid Cancer

Pathological diagnosis remains the gold standard for confirming the diagnosis of thyroid cancer and for guiding clinical decision-making. Histological classification not only determines the cancer subtype but also informs prognosis and treatment strategies. However, differences in diagnostic frameworks across regions and organizations can lead to inconsistencies in classification and interpretation. For example, the General Guidelines for the Description of Thyroid Cancer issued by the Japanese Society of Thyroid Pathology and the Japanese Society of Endocrine Surgery differ from the World Health Organization (WHO) classification in several aspects, notably in the handling of borderline or marginal lesions. The WHO does not formally recognize the category of marginal lesions, which may lead to discrepancies in the diagnosis of low-grade or early-stage malignancies.<sup>44</sup> These inconsistencies highlight the importance of diagnostic standardization and multidisciplinary evaluation in clinical practice.

In recent years, the application of molecular and immunohistochemical markers has enhanced the diagnostic accuracy and risk stratification of thyroid cancer. Specific biomarkers have been shown to provide additional information beyond traditional histopathology. For instance, CALML6 (calmodulin-like protein 6) has been reported to be significantly overexpressed in thyroid cancer tissues and associated with aggressive tumor behavior and high cellularity, which suggests its potential utility as a novel biomarker for identifying high-risk cases and as a candidate for targeted immunotherapy.<sup>45–47</sup>

Furthermore, immunohistochemical staining for proteins involved in tumor invasion and angiogenesis, such as matrix metalloproteinase-9 (MMP-9), vascular endothelial growth factor-C (VEGF-C), and basic fibroblast growth factor (bFGF), has proven helpful in differentiating metastatic from non-metastatic thyroid cancers. Among these, VEGF-C and bFGF have shown the highest diagnostic value for predicting metastatic potential, and their expression levels may serve as prognostic indicators.<sup>48</sup> These markers support more accurate pathological assessment, particularly in cases with indeterminate histology or when evaluating recurrence risk.

From the perspective of TCM, accurate pathological classification is essential for determining the appropriate treatment strategy, particularly when integrating TCM with Western therapies. For example, patients with histologically aggressive or metastatic disease may benefit from TCM interventions aimed at strengthening immune function, reducing tumor burden, and alleviating the side effects of conventional treatments. Moreover, understanding the molecular profile of a tumor may help guide the selection of specific herbal formulations that target pathways such as angiogenesis or apoptosis, which align with TCM principles of resolving phlegm, dissipating masses, and invigorating blood circulation.

In summary, while pathological diagnosis provides the foundation for thyroid cancer classification and treatment planning, the incorporation of molecular markers adds critical information that can enhance precision in clinical care. In the context of integrative medicine, aligning histopathological findings with individualized TCM strategies may offer a more comprehensive and patient-centered approach to the management of thyroid cancer.

## Molecular Diagnosis of Thyroid Cancer

Molecular diagnostic techniques have become an increasingly important supplement to conventional cytological and histological methods in the diagnosis of thyroid cancer, particularly in cases where FNA yields indeterminate or inconclusive results. The ability to detect specific genetic alterations associated with malignancy has significantly improved the preoperative risk stratification of thyroid nodules and has contributed to more individualized treatment

decisions. Key molecular markers frequently analyzed include point mutations in oncogenes such as BRAF and RAS, as well as gene rearrangements involving RET/PTC and PAX8/PPAR $\gamma$ , and these alterations have been closely associated with specific histological subtypes and have been linked to tumor aggressiveness, prognosis, and response to therapy.<sup>48</sup>

Among the most well-established platforms for clinical use is the ThyroSeq v2.1 next-generation sequencing panel, which simultaneously detects a wide array of gene mutations and fusions relevant to thyroid cancer.<sup>49</sup> By providing a comprehensive molecular profile, ThyroSeq improves diagnostic confidence, particularly in nodules classified as Bethesda category III or IV. Although the test has shown promising results in enhancing diagnostic accuracy, further validation in large, diverse populations is necessary before it can be universally adopted as a standard diagnostic tool.

In addition to DNA-based analyses, RNA-based markers, particularly long non-coding RNAs (lncRNAs), have emerged as novel tools with high diagnostic potential. Recent studies have identified specific lncRNA signatures, such as LRR52-AS1, LINC02082, and UNC5B-AS1, that demonstrate high sensitivity (88.9%) and specificity (100.0%) for the detection of papillary thyroid cancer (PTC).<sup>50</sup> These findings underscore the growing role of transcriptomic profiling in refining diagnostic precision, especially in cases where traditional histopathological features may be ambiguous.

From the perspective of TCM, the integration of molecular diagnostics into clinical evaluation holds potential to enhance personalized care. While TCM traditionally relies on symptom patterns, tongue and pulse diagnosis, and syndrome differentiation, molecular profiling may offer a complementary layer of insight into the biological nature of the disease. For example, patients with BRAF mutations or high-risk lncRNA expression patterns may be more likely to benefit from TCM interventions aimed at regulating immune function, clearing heat toxins, and softening masses, principles often applied in managing more aggressive tumor presentations. Moreover, understanding molecular features may help bridge the gap between individualized TCM formulations and emerging molecularly targeted therapies, fostering a more integrative model of care.

In summary, molecular diagnostics represent a valuable advancement in the early and accurate identification of thyroid malignancies. When integrated with clinical, pathological, and even traditional diagnostic approaches, it supports a more holistic understanding of the disease process. This convergence provides an opportunity to align molecular findings with TCM-based treatment principles, paving the way for improved diagnostic precision and tailored therapeutic strategies in the integrative management of thyroid cancer.

## Basic Theory of Thyroid Cancer Treated by TCM

### Analysis of TCM Etiology and Pathogenesis of Thyroid Cancer

TCM posits that the etiology of thyroid cancer is multifactorial. From the perspective of the zang-fu organ theory and meridian pathways, it is particularly associated with liver, spleen, and kidney dysfunction. The liver is responsible for the regulation of qi flow. When emotional disturbances occur, liver function may become impaired, leading to qi stagnation. This stagnation can subsequently transform into heat, resulting in the condensation of bodily fluids into phlegm, which may obstruct the neck and contribute to the formation of tumors. When deficient, the spleen, which governs the processes of transportation and transformation, can lead to abnormal fluid dynamics, causing the retention of dampness and the subsequent generation of phlegm. This accumulation can exacerbate qi stagnation and tumor development. The kidneys, regarded as the source of innate vitality, when deficient in yin, may experience an inflammatory response due to a deficiency of fire, which can convert bodily fluids into phlegm, thereby facilitating the accumulation of both phlegm and heat, potentially leading to thyroid cancer.<sup>9</sup>

Numerous mutations have been identified at the genetic level in patients with thyroid cancer in China. Notably, BRAF driver mutations were present in 76.0% of the cases, RET rearrangements in 7.6%, and RAS driver mutations in 4.1%. The prevalence of somatic mutations has been correlated with various clinical characteristics, including patient age, tumor differentiation, size, and the presence of lymph nodes or distant metastases.<sup>51</sup> TCM suggests that these genetic alterations may be linked to a deficiency in healthy qi and the invasion of external pathogens, which disrupts the circulation of qi and blood and impairs organ function, ultimately contributing to the onset and progression of tumors.

## Theoretical Basis of TCM in the Treatment of Thyroid Cancer

The treatment of thyroid cancer in TCM is based on a holistic understanding of the human body and the principle of syndrome differentiation.<sup>52</sup> TCM views the body as an interconnected system, where organs, energy (qi), blood, and meridians work together to maintain health.<sup>52</sup> Although thyroid cancer appears as a localized disease in the neck, TCM considers it a result of deeper imbalances involving the liver, spleen, and kidney.<sup>53</sup> For example, emotional stress can affect liver function and cause stagnation of qi, leading to the formation of phlegm and nodules.<sup>54</sup> Weakness of the spleen may impair fluid metabolism, contributing to further accumulation of phlegm.<sup>55</sup> Kidney deficiency may also reduce the body's ability to regulate heat and fluids, worsening internal imbalances.<sup>56</sup> Overall, TCM treatment aims to restore the balance between yin and yang, improve the circulation of qi and blood, remove phlegm, and support organ function, and by doing so, it seeks to strengthen the body's natural ability to fight cancer.

In recent years, studies have shown that TCM may influence cancer development through several biological pathways.<sup>5</sup> Some herbal compounds can slow the growth of thyroid cancer cells by interfering with their ability to multiply.<sup>28</sup> Others can trigger cancer cell death by activating related genes and proteins.<sup>57</sup> TCM has also been reported to reduce the formation of new blood vessels that supply nutrients to tumors, thereby limiting tumor growth and spread.<sup>51</sup>

Additionally, TCM may improve the immune response by increasing the activity of immune cells such as T cells and natural killer (NK) cells, which help the body detect and destroy cancer cells.<sup>58</sup> Some studies also suggest that TCM can reduce damage to healthy cells by limiting inflammation and protecting genetic material from harmful changes.<sup>59</sup> Taken together, TCM provides a treatment approach that focuses not only on the tumor itself but also on improving the body's internal environment and overall condition, which has shown efficacy in helping relieve symptoms, support recovery, and improve the patient's quality of life when used alongside standard medical care.

## Comparison of TCM and Western Medicine in the Treatment of Thyroid Cancer

The treatment of thyroid cancer within the framework of Western medicine primarily encompasses surgical intervention, chemotherapy, radiotherapy, radioactive iodine therapy, and targeted therapy. Surgical procedures are considered the principal modality, as they facilitate the excision of tumor tissue; however, they may lead to postoperative complications such as hypothyroidism and some may experience postoperative regrets.<sup>60</sup> Chemotherapy and radiotherapy exert a direct cytotoxic effect on cancer cells, yet they also pose the risk of damaging normal tissues, resulting in a range of adverse effects.<sup>61</sup> Radioactive iodine therapy is indicated for differentiated thyroid cancer, although some patients may develop resistance to this treatment. Targeted therapy demonstrates efficacy against specific molecular targets; however, challenges such as drug resistance and associated side effects persist.<sup>62</sup>

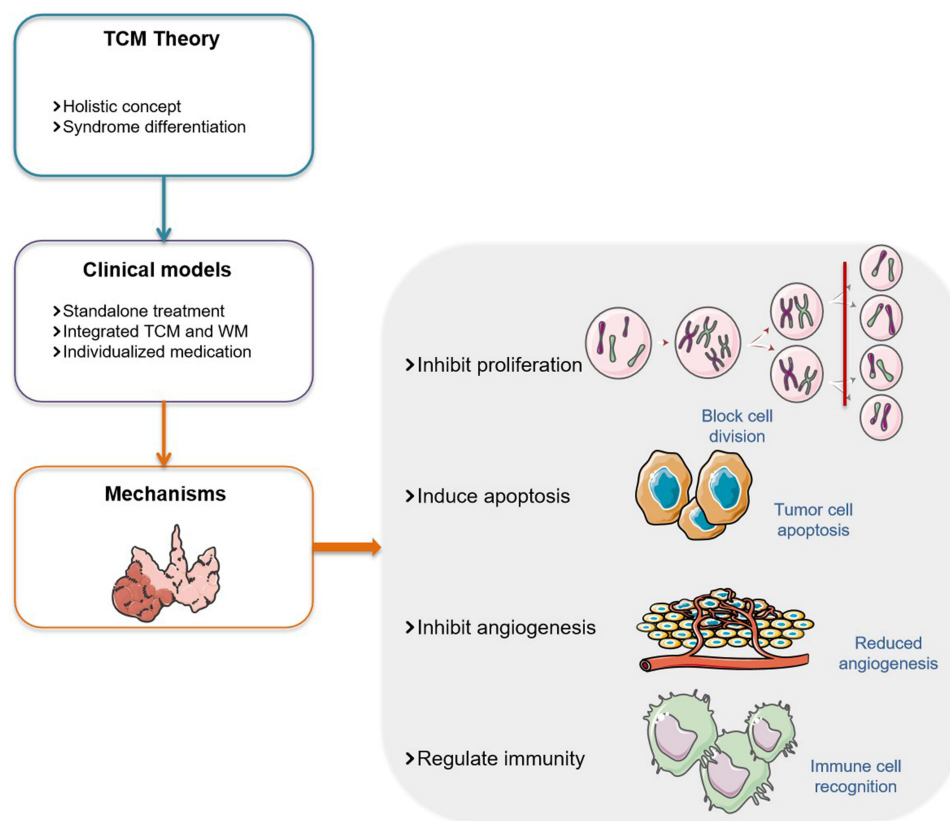
In contrast, the approach of TCM for thyroid cancer emphasizes holistic conditioning and is associated with relatively minimal side effects. TCM aims to regulate the body's internal environment and bolster its inherent anticancer capabilities, thereby inhibiting tumor growth, alleviating symptoms, and enhancing the overall quality of life. However, the therapeutic effects of TCM may manifest more gradually, and its efficacy in local tumor control may not match that of Western medical interventions. In clinical practice, a synergistic approach that integrates both Traditional Chinese and Western medicine is beneficial. Western medicine can swiftly manage tumor progression, whereas TCM can mitigate the adverse effects of Western treatments, improve patient quality of life, enhance immune function, and help prevent tumor recurrence and metastasis.<sup>9</sup>

The basic theory of comprehensive TCM treatment of thyroid cancer is summarized as follows, as shown in [Figure 2](#).

## Application of TCM in the Diagnosis of Thyroid Cancer

### TCM Diagnosis of Thyroid Cancer

In TCM, the diagnostic assessment of thyroid cancer is based on the classical diagnostic methods of inspection, auscultation, olfaction, inquiry and palpation to identify patterns of internal imbalance through the observation of external manifestations and patient-reported symptoms.<sup>63</sup> During inspection, TCM practitioners carefully evaluate the characteristics of neck masses, including their shape, size, texture, and color.<sup>63</sup> A mass that appears hard, fixed, and irregular in contour may raise suspicion for malignancy. Additionally, tongue inspection provides insight into internal conditions;<sup>64</sup> for instance, a dark or purplish



**Figure 2** Conceptual framework of Traditional Chinese Medicine (TCM) theory in thyroid cancer management.

complexion with a thick, greasy tongue coating may suggest the presence of phlegm retention and blood stasis, which are essential pathological factors commonly associated with tumor formation in TCM theory.

Auscultation and olfaction assessments aim to evaluate vocal quality and breath odor.<sup>63</sup> The presence of hoarseness may indicate potential involvement of the recurrent laryngeal nerve by the tumor, while abnormal odors may reflect internal heat or toxin accumulation.<sup>65</sup> Further assessments involve detailed questioning about the patient's symptoms, including the onset and progression of neck discomfort, dysphagia, shortness of breath, systemic fatigue, and changes in appetite or weight. It also includes reviewing the patient's medical and family history to identify contributing constitutional or hereditary factors. Palpation of the neck is used to assess the mass's texture, tenderness, mobility, and relationship to surrounding tissues. When this is combined with pulse diagnosis, such as the presence of a wiry or slippery pulse, TCM practitioners may deduce patterns such as qi stagnation, phlegm accumulation, or blood stasis.<sup>66</sup>

Despite the long-standing use of these diagnostic methods, one of the key limitations of TCM-based diagnosis is its inherent subjectivity and the absence of standardized, quantitative criteria.<sup>66</sup> As a result, the sensitivity and specificity for detecting early-stage thyroid cancer or distinguishing between benign and malignant lesions remain limited. Moreover, the lack of imaging or histological validation makes it challenging to assess tumor size, invasion, or metastasis accurately. Therefore, integrating modern diagnostic techniques, including ultrasound, cytology, and molecular testing, into the TCM diagnostic framework is essential for improving diagnostic precision and supporting more effective, individualized treatment planning.

## Progress in Diagnosis of TCM Combined with Modern Technology

Recent advancements in biomedical science and technology have created new opportunities to integrate TCM with modern diagnostic tools to improve the precision and applicability of TCM in the diagnosis and management of thyroid cancer and address the limitations of traditional diagnostic methods by incorporating objective, quantifiable data and enhancing the molecular understanding of disease processes.

One such advancement is the application of nanotechnology, which enables the conversion of active components from traditional herbal formulations into nano-scale delivery systems, and these nano-formulations not only improve the bioavailability and stability of TCM compounds but also enhance their ability to selectively accumulate in tumor tissues.<sup>67</sup> When administered via nanocarriers, these formulations can be used not only for therapeutic purposes but also for diagnostic imaging and tumor monitoring, allowing for more targeted identification of thyroid lesions.<sup>67</sup> Such innovations are paving the way for the development of dual-purpose theranostic agents that combine both diagnostic and therapeutic functions, increasing the clinical utility of TCM in oncology.

In parallel, the fields of network pharmacology and bioinformatics have provided powerful platforms for analyzing the complex interactions between TCM compounds and disease-related targets. By constructing TCM target-disease interaction networks, researchers can systematically identify the active ingredients in TCM formulations, their molecular targets, and the signaling pathways involved in thyroid cancer pathogenesis.<sup>68</sup> This approach has not only improved our understanding of how multi-component TCM therapies exert their effects but has also led to the identification of potential diagnostic biomarkers and therapeutic targets. For instance, mapping the interactions between herbal compounds and key oncogenic pathways, such as MAPK, PI3K/AKT, and VEGF signaling, can help validate the relevance of TCM in modern thyroid cancer care.<sup>68</sup>

Moreover, these computational tools allow for the prediction of synergistic mechanisms between multiple TCM ingredients, supporting the formulation of evidence-based compound prescriptions, which enhances the scientific basis for individualized diagnosis and treatment in TCM, moving beyond traditional empirical approaches.<sup>69</sup> Importantly, by combining these modern techniques with TCM principles of syndrome differentiation, clinicians may develop more refined diagnostic models that incorporate both subjective clinical presentation and objective molecular evidence.

In summary, the integration of modern technologies with TCM diagnostic principles has opened new avenues for the accurate identification and understanding of thyroid cancer. These advancements not only validate traditional diagnostic frameworks but also support their evolution into more precise and clinically relevant systems, aligning with contemporary standards of personalized and integrative cancer care.

## Advantages and Limitations of TCM in the Diagnosis of Thyroid Cancer

TCM offers a distinct diagnostic perspective rooted in the principles of holistic assessment and syndrome differentiation. Unlike organ-specific evaluations typical of Western diagnostics, TCM emphasizes the interconnection between bodily systems, allowing practitioners to evaluate not only the localized presentation of a thyroid mass but also the patient's broader physiological and constitutional state.<sup>70</sup> This approach enables early identification of underlying imbalances, such as qi stagnation, phlegm accumulation, or blood stasis, that may predispose to or accompany thyroid cancer.<sup>71</sup> Such individualized assessments form the basis for early, preventive, and tailored interventions, which are particularly relevant in the context of integrative cancer care.

In clinical practice, TCM diagnostic techniques, comprising inspection, palpation, tongue and pulse diagnosis, and inquiry, are non-invasive, easy to perform, and generally well accepted by patients. These methods allow for repeated, real-time evaluations of the patient's condition and can guide dynamic adjustments in treatment planning. Moreover, certain Chinese herbal formulations traditionally used for resolving nodules, regulating qi, and invigorating blood have shown potential not only for symptom management but also for supporting early-stage intervention.<sup>9</sup> When integrated thoughtfully with modern diagnostic tools, these techniques may enhance the overall sensitivity of a multimodal diagnostic approach.

However, despite these advantages, TCM-based diagnostic methods face important limitations. One major challenge is the lack of standardized, objective criteria for diagnosis. Clinical judgments often rely heavily on practitioner experience, leading to variability in interpretation and potentially inconsistent diagnostic outcomes. This subjectivity limits the reproducibility and generalizability of TCM diagnoses, especially in complex cases such as early-stage or small thyroid cancers (microcarcinomas), where subtle clinical signs may be overlooked.<sup>52</sup> Furthermore, traditional TCM methods are insufficient for accurately determining tumor size, location, invasiveness, or metastatic status, critical parameters for treatment decision-making and prognosis.

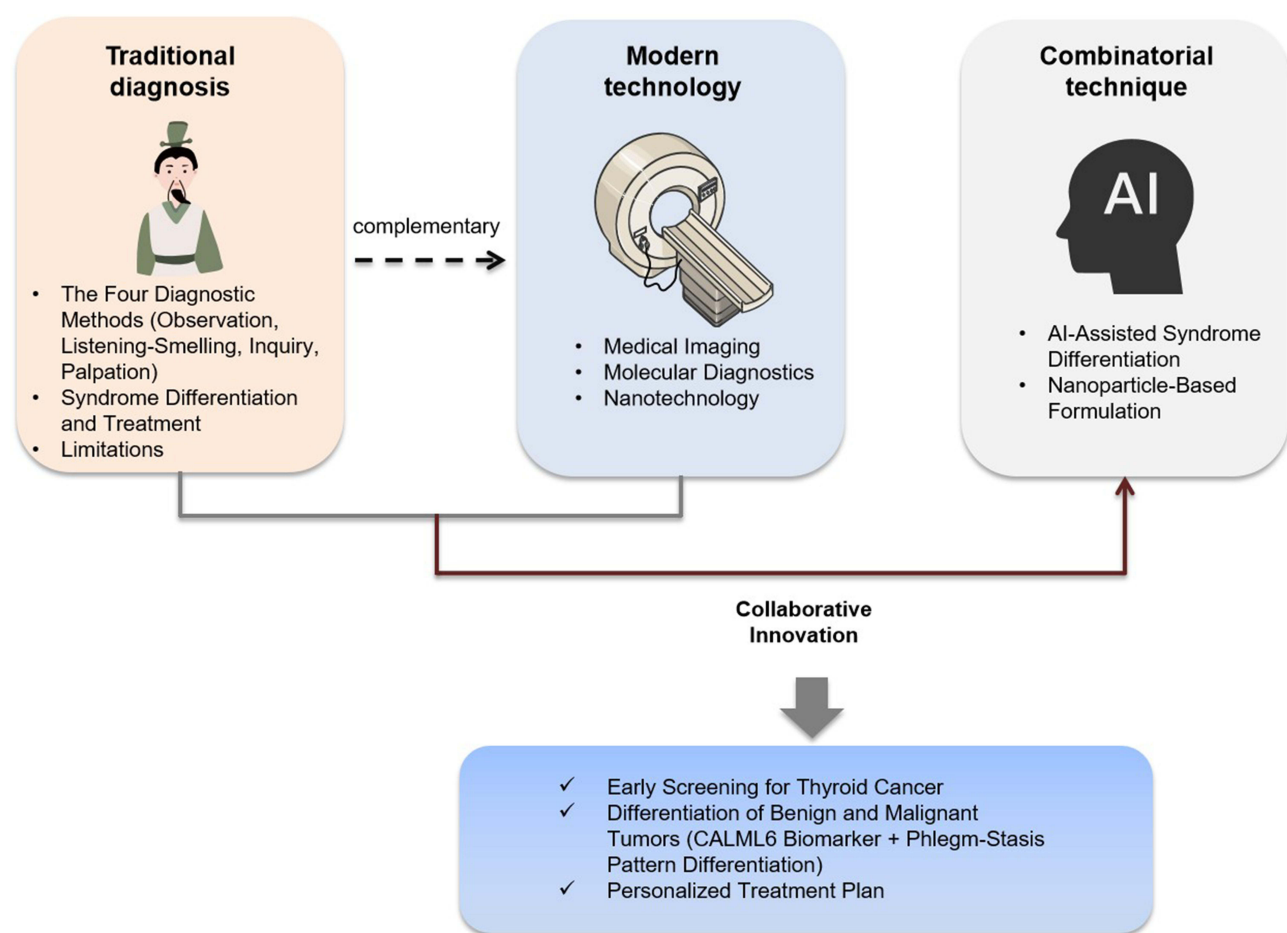
Currently, there is also a lack of high-quality, large-scale clinical studies evaluating the diagnostic accuracy of TCM in thyroid cancer. Most available evidence is descriptive or anecdotal, and rigorous validation through multicenter research is lacking. Addressing this gap will be essential to establish the clinical reliability of TCM as a diagnostic tool and clarify its role alongside imaging, cytology, and molecular diagnostics. Overall, while TCM provides a valuable patient-centered and symptom-driven framework for thyroid cancer assessment, its diagnostic application should be viewed as complementary rather than standalone. Integrating TCM insights with modern diagnostic technologies holds promise for improving diagnostic precision and personalizing care. A visual summary of the diagnostic advantages and constraints of TCM is provided in Figure 3.

## Clinical Practice of Thyroid Cancer Treated by TCM

### Clinical Studies on Thyroid Cancer Treated by TCM Monotherapy

The application of TCM as a standalone therapeutic approach in thyroid cancer management has attracted increasing attention, particularly for its potential in symptom relief and quality-of-life improvement. TCM monotherapy is often guided by syndrome differentiation, with treatment regimens targeting internal imbalances such as phlegm-qi stagnation and blood stasis, which are believed to underlie the pathogenesis of neck masses in the TCM framework.

One clinical study by Jeon et al investigated the efficacy and safety of acupuncture for radioactive iodine (RAI)-induced anorexia in thyroid cancer patients. This randomized, double-blinded, sham-controlled pilot study enrolled 14 patients who were randomly assigned to receive either true or sham acupuncture over a two-week period. Although both groups showed improvement in anorexia-related symptoms, the true acupuncture group exhibited statistically significant



**Figure 3** Diagnostic application of Traditional Chinese Medicine (TCM) in thyroid cancer.

improvements in specific quality-of-life subscales, including the Trial Outcome Index (TOI), Functional Assessment of Cancer Therapy–General (FACT-G), and Functional Assessment of Anorexia and Cachexia Therapy (FAACT) scores ( $P < 0.05$ ). Importantly, no serious adverse events were reported, highlighting acupuncture’s potential as a safe and supportive monotherapy for alleviating RAI-induced side effects and enhancing well-being in thyroid cancer patients.<sup>72</sup>

In addition, a recent clinical observation conducted by Li et al assessed the therapeutic efficacy of a traditional compound formula, Fufangbanmao capsule, when used alone or in combination with the CAF chemotherapy regimen in patients with thyroid cancer following radical surgery. Among 118 patients enrolled, those in the experimental group who received the combined treatment demonstrated superior objective response rate (ORR, 91.53%) and disease control rate (DCR, 96.61%) compared to the control group receiving CAF alone (ORR, 76.27%; DCR, 83.05%) ( $P = 0.024$  and  $P = 0.015$ , respectively). Moreover, the experimental group exhibited significant improvements in immune parameters, including CD3+, CD4+, CD8+, CD4+/CD8+ ratios, and NK cell levels ( $P < 0.001$  for all), along with enhanced scores across several dimensions of quality of life. While no statistically significant differences in toxicity profiles were observed between the groups, patients receiving the TCM combination reported fewer adverse drug reactions, suggesting a potential protective role of Fufangbanmao in mitigating chemotherapy-related side effects.<sup>73</sup>

In broader evidence synthesis, a systematic review of 5,834 randomized controlled trials on cancer-related therapies found that approximately 18.55% employed TCM monotherapy for symptom control and side-effect management. Among these, a subset of trials specifically addressed thyroid cancer, providing preliminary support for the palliative efficacy of TCM in improving daily function and reducing symptom burden.<sup>74</sup>

Despite these encouraging findings, several limitations must be acknowledged. The majority of available clinical studies on TCM monotherapy for thyroid cancer are constrained by small sample sizes, single-center designs, and inconsistent methodological standards. These factors hinder the generalizability and reproducibility of findings. Consequently, there remains an urgent need for high-quality, large-scale, multicenter clinical trials employing rigorous randomized and controlled methodologies to confirm the clinical efficacy and long-term safety of TCM monotherapy in thyroid cancer management.

## Clinical Effect of Integrated Traditional Chinese and Western Medicine in the Treatment of Thyroid Cancer

The integration of TCM with Western medical practices for the treatment of thyroid cancer has emerged as a prevalent clinical approach, yielding favorable clinical outcomes. In a study involving 120 patients diagnosed with thyroid cancer, the participants were allocated into two groups: the experimental group, which received total thyroidectomy in conjunction with radioactive iodine therapy, and the control group, which underwent traditional total thyroidectomy alone. The findings indicated that the overall efficacy rate in the experimental group surpassed that in the control group. Furthermore, assessments of quality of life revealed that the experimental group exhibited significantly superior scores in physiological function, psychological function, social function, and overall quality of life compared with the control group.<sup>75</sup>

Additionally, a separate investigation focusing on benign thyroid nodules demonstrated that patients receiving a combination of TCM and Western medicine achieved a higher efficacy rate. Post-treatment evaluations indicated a reduction in maximum nodule diameter and thyroid volume, along with decreased serum levels of free triiodothyronine (FT3), free thyroxine (FT4), and TSH. Moreover, scores related to TCM syndromes have diminished.<sup>76</sup> Collectively, these studies underscore the potential of integrated traditional Chinese and Western medical treatments to enhance therapeutic outcomes for thyroid cancer and improve patients’ quality of life.

## Individualized Program of TCM for Thyroid Cancer

TCM emphasizes the principle of individualized treatment, wherein therapeutic regimens are formulated based on the patient’s unique constitutional characteristics, clinical manifestations, and syndrome differentiation, and this tailored approach reflects one of the core strengths of TCM in managing complex conditions such as thyroid cancer.<sup>77</sup> Unlike standardized protocols common in Western medicine, TCM treatments are dynamically adjusted according to both disease progression and patient responsiveness, allowing for more flexible and holistic care.

In clinical practice, patients with thyroid cancer often exhibit distinct patterns of internal disharmony, which are interpreted through the TCM diagnostic framework. For example, individuals presenting with liver depression and qi stagnation, a common pattern characterized by emotional stress, irritability, and nodular formations, are typically treated with a modified version of Chaihu Shugan Powder.<sup>78</sup> This formulation is intended to soothe the liver, regulate qi, resolve phlegm, and dissipate localized masses. For patients whose presentations are dominated by phlegm accumulation and blood stasis, a modified Haizao Yuhu Decoction is employed.<sup>79</sup> This prescription focuses on promoting blood circulation, dispersing phlegm, and softening firm masses, which correspond pathophysiologically to tumor growth in TCM theory.

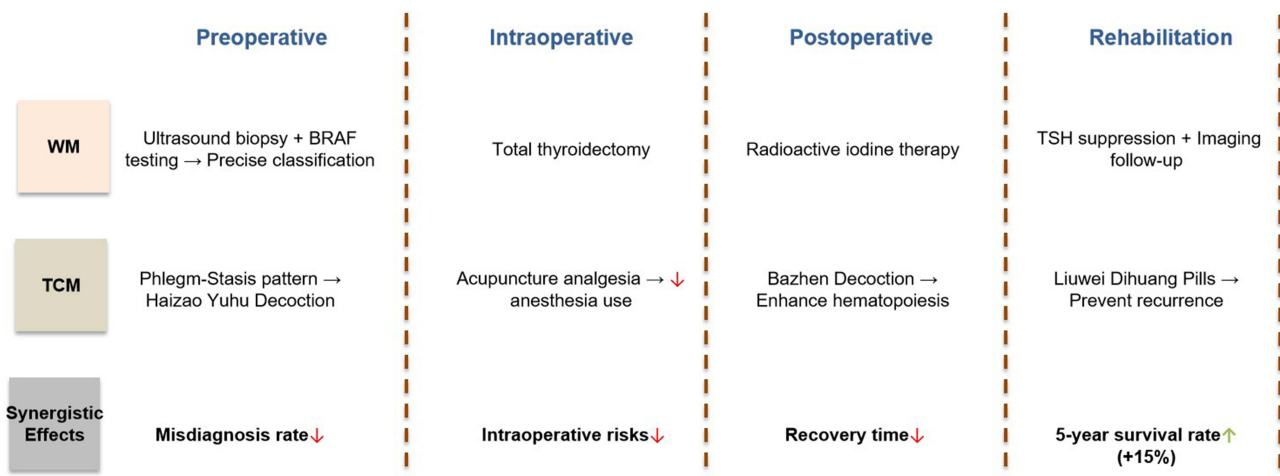
For patients experiencing dual deficiencies of qi and yin, often associated with fatigue, dry mouth, palpitations, or night sweats, clinical strategies aim to tonify qi, nourish yin, and simultaneously target the tumor mass.<sup>71</sup> Importantly, advances in molecular biology have further supported the refinement of individualized TCM strategies. The integration of genetic testing and molecular profiling from modern oncology into TCM decision-making represents a promising area of translational integration.<sup>80</sup> For instance, in patients with confirmed BRAF mutations, commonly associated with aggressive thyroid cancers, TCM treatments can be adapted to focus on heat-clearing and detoxification methods,<sup>28</sup> which are traditionally used to suppress tumor proliferation. This form of integrative precision medicine enables TCM practitioners to tailor herbal prescriptions more effectively, potentially enhancing therapeutic efficacy and reducing adverse effects.

Moreover, the flexibility of TCM allows for real-time adjustments in herbal composition and dosage based on treatment response and patient tolerance.<sup>81</sup> Such dynamic modulation not only contributes to the long-term management of thyroid cancer but also improves patients' quality of life by addressing symptoms such as pain, fatigue, and psychological distress, dimensions often under-addressed in conventional cancer care. A summary of individualized TCM treatment strategies for thyroid cancer is illustrated in Figure 4.

## Technical Progress of TCM in the Treatment of Thyroid Cancer

### Application of New TCM in the Treatment of Thyroid Cancer

Recent advancements in TCM formulations have offered promising prospects for the treatment of thyroid cancer. Certain bioactive compounds derived from TCM can be transformed into innovative preparations, including nanoformulations, liposomes, and microspheres, through extraction, purification, and enhancement of the preparation techniques. These modifications can significantly enhance bioavailability and targeting of therapeutic agents. For instance, the conversion of TCM active ingredients into nanoparticles with a reduced particle size has been shown to increase drug accumulation within tumor tissues, thereby improving therapeutic efficacy while minimizing damage to adjacent healthy tissues.<sup>67</sup>



**Figure 4** Clinical strategies of Traditional Chinese Medicine (TCM) treatment for thyroid cancer.

**Notes:** Red arrow: ↓ Misdiagnosis (Pre-op WM/TCM). Green arrow: ↑ 5-year survival ↑15% (Full pathway).

**Abbreviations:** WM, Western Medicine; TCM, Traditional Chinese Medicine.

Research indicates that these novel TCM preparations may exert anticancer effects through multiple mechanisms. They have been found to effectively inhibit the proliferation and metastasis of thyroid cancer cells by promoting apoptosis and suppressing angiogenesis. Furthermore, these preparations may also modulate immune function, thereby bolstering the body's resistance to tumor development. Nonetheless, the application of these new TCM formulations for the treatment of thyroid cancer remains largely investigational, necessitating further clinical trials to establish their safety and efficacy.

## Innovative Therapy Combining TCM with Modern Technology

Integration of TCM with contemporary technological advancements has led to the emergence of various innovative therapeutic approaches. Notably, the application of nanotechnology in TCM has facilitated the development of a nano-targeted delivery system that enables the precise administration of active constituents found in TCM, thereby enhancing therapeutic efficacy. For instance, nanocarriers can specifically transport the active components of TCM to thyroid cancer cells, thereby augmenting the cytotoxic effects on malignant cells while minimizing the adverse effects on healthy cells.<sup>82</sup>

Furthermore, network pharmacology and bioinformatics have introduced novel strategies for the treatment of thyroid cancer using TCM. By examining the interactions between the active ingredients of TCM and targets associated with thyroid cancer, researchers can identify specific compounds with potential anticancer properties, thereby laying the groundwork for the development of new pharmacological agents and optimization of treatment protocols. Additionally, artificial intelligence technologies can support the differentiation of TCM syndromes and treatment modalities, enhance diagnostic accuracy, and standardize therapeutic interventions.

## Prospect of TCM in the Treatment of Thyroid Cancer

In the foreseeable future, advancements in the treatment of thyroid cancer through TCM are anticipated across various technical domains. Gene editing technologies, such as CRISPR-Cas9, can be employed to investigate the regulatory mechanisms by which TCM influences genes associated with thyroid cancer, thereby providing a theoretical foundation for the development of targeted therapeutic agents. For instance, by utilizing CRISPR-Cas9 to knockout or modify critical genes implicated in thyroid cancer, researchers can assess the impact of TCM on gene expression and functionality, thereby gaining a deeper understanding of the anticancer mechanisms inherent in TCM.<sup>83</sup>

Furthermore, the integration of stem cell therapy with TCM has significant potential. Stem cells possess unique capabilities of self-renewal and differentiation, enabling them to repair damaged tissues and modulate immune responses. TCM can influence the proliferation and differentiation of stem cells, thereby enhancing their therapeutic efficacy. For example, TCM may facilitate the differentiation of mesenchymal stem cells into thyroid cells, thereby aiding in the restoration of thyroid function and contributing to anticancer effects. Additionally, ongoing advancements in nanotechnology are expected to yield nano-formulations of TCM that are more precise and effective, potentially leading to novel breakthroughs in the treatment of thyroid cancer.

## Controversies and Challenges in the Treatment of Thyroid Cancer with TCM

### Controversy Over the Safety and Effectiveness of TCM in the Treatment of Thyroid Cancer

The safety and efficacy of TCM in the management of thyroid cancer remain a subject of debate. While the adverse effects associated with TCM are generally minimal, certain formulations may induce negative reactions, including hepatotoxicity, nephrotoxicity, and allergic responses. For example, TCMs containing aristolochic acid have been linked to renal impairment. Furthermore, the therapeutic quality of TCM is influenced by various factors, including the source of the ingredients and methods of preparation, which can lead to inconsistencies in quality that may compromise both efficacy and safety.<sup>84</sup>

In terms of efficacy, although some clinical investigations suggest that TCM may play a role in alleviating symptoms and enhancing the quality of life of patients with thyroid cancer, there is a notable absence of large-scale, multicenter,

randomized controlled trials to substantiate its definitive effectiveness. Many studies are characterized by small sample sizes and methodological limitations, which undermine the reliability and persuasiveness of their findings. Additionally, the underlying mechanisms by which TCM exerts its effects in the treatment of thyroid cancer remain poorly understood, further hindering its broader clinical application.<sup>85</sup>

## Standardization of TCM Treatment of Thyroid Cancer

Standardization of TCM for the management of thyroid cancer presents numerous challenges. There is a lack of uniform quality standards for traditional Chinese medicinal products, resulting in variability in the concentration of active ingredients and pharmacological effects among different batches and sources. This inconsistency can adversely affect the reliability of clinical outcomes. For instance, the concentration of ginsenosides in ginseng is significantly influenced by geographical origin and harvest season.

Moreover, TCM treatment approaches predicated on syndrome differentiation do not adhere to standardized protocols, leading to potential discrepancies in treatment regimens among practitioners for the same patient. Additionally, there is an absence of uniform guidelines regarding the treatment duration and dosages of TCM for thyroid cancer, with practitioners often relying on personal experience to devise treatment plans. This reliance on subjective judgment may hinder the broader acceptance and implementation of TCM in the treatment of thyroid cancer.<sup>86</sup>

## Ethical and Regulatory Challenges of TCM in the Treatment of Thyroid Cancer

TCM currently encounters ethical and regulatory challenges in the management of thyroid cancer. From an ethical perspective, the application of TCM raises concerns regarding patients' right to information and autonomy in decision-making. The intricate mechanisms underlying TCM treatment may lead to a lack of understanding among patients regarding their treatment plans, thereby impeding their ability to make informed choices. Furthermore, in the context of clinical trials involving TCM, safeguarding the rights and interests of participants while ensuring scientific rigor and ethical integrity of the trials remains a significant concern.<sup>87</sup>

The existing framework governing TCM is inadequate in terms of regulatory oversight. The process for the approval of new drug research and development within TCM is notably complex, and there is a deficiency in the established evaluation criteria that account for the unique characteristics of TCM. Additionally, the TCM market is plagued by issues such as counterfeit products and unauthorized additives, which compromise the quality and safety of these treatments. Therefore, enhancing the ethical review processes and regulatory oversight of TCM in the treatment of thyroid cancer, along with the development of relevant laws, regulations, and standards, is essential for promoting the responsible application of TCM.

## Conclusion

This review summarized current evidence on the application of TCM in the diagnosis and treatment of thyroid cancer, highlighting its theoretical foundations, therapeutic mechanisms, clinical applications, and integration with modern technologies. TCM emphasizes a holistic and individualized approach, guided by syndrome differentiation, and has demonstrated potential in improving symptom control, enhancing quality of life, and reducing adverse effects associated with conventional therapies. Both monotherapy and combination regimens involving TCM have shown promising outcomes in small-scale clinical studies, particularly in alleviating radioactive iodine-induced complications, reducing tumor burden, and modulating immune function. Advances in molecular diagnostics, network pharmacology, and nanotechnology have further enabled the modernization and precision of TCM-based interventions. These approaches offer new opportunities to identify therapeutic targets, elucidate pharmacodynamic mechanisms, and improve the specificity of TCM formulations. Additionally, TCM's strengths in early symptom recognition and patient-tailored regimens present complementary value to modern diagnostic and therapeutic protocols.

Nonetheless, several limitations remain. Many existing studies suffer from small sample sizes, methodological heterogeneity, and a lack of long-term follow-up, limiting the generalizability and strength of current evidence. There is an urgent need for high-quality, large-scale, multicenter randomized controlled trials to validate the efficacy and safety

of TCM interventions in thyroid cancer. Moreover, future research should continue exploring the integration of molecular profiling and individualized TCM strategies to enhance therapeutic precision and clinical outcomes.

Thus, while TCM offers valuable complementary perspectives and treatment modalities for thyroid cancer, its clinical application must be supported by rigorous scientific validation and standardized practice guidelines. The integration of traditional and modern medical approaches holds considerable potential to advance personalized, effective, and holistic care for patients with thyroid cancer.

## Abbreviations

PTC, papillary thyroid cancer; FTC, follicular thyroid cancer; PDTC, poorly differentiated thyroid cancer; ATC, anaplastic thyroid cancer; WDTC, well-differentiated thyroid cancers; TSH, thyroid-stimulating hormone; RAI, radioiodine therapy; ATC, anaplastic thyroid cancer; TCM, Traditional Chinese medicine; CSCs, cancer stem-like cells; EMT, epithelial-mesenchymal transition; MTC, medullary thyroid cancer; SNPs, single nucleotide polymorphisms; HDI, Human Development Index; TgAb, thyroglobulin antibodies; FNMTC, familial non-medullary thyroid cancer; FDG, fluorodeoxyglucose; WHO, World Health Organization; RNAs, long non-coding, lncRNAs; FT3, free triiodothyronine; FT4, free thyroxine.

## Funding

Harbin City Science and Technology self-raised funding project (2023ZCZJNS108); Harbin Science and Technology Self-raised Funds Project Harbin Science and Technology Self-Raised Funds Project (2023ZCZJNS108).

## Disclosure

The authors declare that they have no affiliations with or involvement in any organization or entity with any conflicts of interest in the subject matter or materials discussed in this manuscript.

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