

Advances in Nasopharyngeal Carcinoma Research from the Perspective of Integrated Traditional Chinese and Western Medicine: From Traditional Wisdom to Molecular Mechanisms

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Abstract: NPC is a geographically clustered head and neck cancer driven by EBV, genetics, and environment. Western medicine uses radiotherapy, chemotherapy, targeted therapy, and immunotherapy based on staging; advances include IMRT, AJCC 9th edition, and immune checkpoint inhibitors. TCM classifies NPC as “nasal sinusitis” or “malignant nodule”, attributing it to toxinstasisphlegm with underlying deficiency, and focuses on supporting healthy qi and syndrome differentiation. Evidence shows TCM injections boost CD3⁺/CD4⁺ T cells; Qingdu Zengye Decoction induces apoptosis via PI3KAkt; the “toxinpermeating and roottonifying” approach links TCM to efferocytosis to counter resistance and immune escape. Integrated medicine offers mutual synergy, not simple addition. This review summarizes progress and future directions.

Keywords: nasopharyngeal carcinoma; integrated ChineseWestern medicine; radiotherapy; traditional Chinese medicine injection; network pharmacology; immune microenvironment

1. Introduction

Nasopharyngeal carcinoma (NPC) is an epithelial cancer arising from the fossa of Rosenmüller, with ~133,000 new cases and 80,000 deaths annually[1]. It shows striking geographic clustering, especially in southern China (15–50 per 100,000), earning the name “Cantonese cancer.” Even highrisk migrants retain elevated incidence, highlighting genetic susceptibility[2]. Etiologically, NPC is driven by multifactorial interactions. EBV infection is a core driver (detectable in >70% of tissues). In highincidence areas, EBV antibody profiles enable early screening. Genetic background (e.g., HLA polymorphisms), environmental exposures (smoking, alcohol, high nickel), and preserved food intake are also risk factors. Alcohol (>15 drinks/week) is a key modifiable risk. The concealed anatomy near the skull base limits surgery, making radiotherapy the only curative modality. Over 70% of patients present with locally advanced disease[2]. TCM plays a supportive role, though “nasopharyngeal carcinoma” is absent in classical texts — its descriptions are scattered under terms like “epistaxis,” “true headache,” and “malignant nodule,” reflecting symptombased tradition and creating integration challenges.

2. Advances in Western Medicine Research

2.1 Precision in Diagnosis and Staging Systems

NPC diagnosis is confirmed by biopsy under nasoendoscopy. CT and MRI are used to assess tumor extent, while FDG-PET/CT is for systemic screening in N2–N3 or suspected distant metastasis. On January 1, 2025, the AJCC 9th edition staging was implemented. The key N-stage change: patients with severe extracapsular extension (grade 3) are now upgraded to N3. For T-stage: only osteosclerosis without definite tumor invasion is not considered skull base invasion; imaging evidence of cranial nerve or infraorbital fissure invasion is T4. The new staging system is more precise: stage IA (T1–2N0), IB (T1–2N1), previous stage III downgraded to II, previous IVA downgraded to III, and stage IV reserved for metastatic cases (M1A ≤3 lesions, M1B >3 lesions)[3].

2.2 Continuous Evolution of Radiotherapy Technology

NPC is highly sensitive to radiotherapy. In the 2D radiotherapy era, 5year survival was below 50%, with damage to the middle ear, temporal lobe, and optic nerve. IMRT changed this: it delivers higher tumor doses while reducing radiation to nearby organs [4]. Heidelberg data showed IMRT plus weekly cisplatin achieved 96% 5year survival with no severe side effects [2]. A 10year study found chemoradiotherapy improved survival by ~29% and 26% over IMRT alone. In September 2025, an international guideline led by Dr. Jun Ma addressed eight key challenges in target delineation, such as tumor extension and postchemo lymph node irradiation [4]. However, weight loss and position changes during 6–7 weeks of treatment can cause errors, making adaptive radiotherapy a current research focus [3].

2.3 Standardization and Exploration of Combined Modality Therapy

Stagebased treatment is clinical consensus: earlystage NPC responds well to radiotherapy ± chemotherapy; locally advanced disease typically receives induction chemotherapy followed by concurrent chemoradiotherapy (CCRT) or CCRT with adjuvant chemotherapy. Platinumbased chemotherapy has a 50–80% firstline response rate. Recent advances in targeted therapy (nimotuzumab) and immunotherapy (PD1/PDL1 inhibitors) are reshaping treatment for advanced NPC [3]. However, despite improved longterm survival, recurrence and metastasis remain major barriers – distant metastasis is the predominant failure pattern, especially in N3 patients[2].

3. Advances in Traditional Chinese Medicine Research

3.1 Theoretical Basis of Disease Differentiation and Syndrome Differentiation

Classical TCM lacks a specific name for NPC, but symptoms appear under terms like “true headache” and “malignant nodule.” Professor Tian Daofa defined the core pathogenesis as “qi deficiency with toxin infection, yang depletion and yin binding,” and the principle of “supporting healthy qi to eliminate pathogens.” He divided progression into two stages: early (qi deficiency, treated with Yiqi Jiedu Fang) and late (yang deficiency with stasis, treated with Yiqi Wenyang Huoxue Fang paralleling Western staging[5]. Clinical studies describe five NPC syndromes. A 2025 imagingTCM study (138 untreated patients) found: liverstagnation with phlegm (39.9%), heattoxin in lung (21.7%), qistagnation with blood stasis (18.8%), and qiyin deficiency (19.6%). Qiyin deficiency was linked to parapharyngeal space invasion, eustachian tube cushion invasion, and distant metastasis. These correlations help standardize TCM syndrome differentiation.

3.2 Molecular Mechanisms of TCM Compound Formulas

Recent advances in network pharmacology and singlecell transcriptomics have shifted TCM mechanism research from empirical to molecular levels. In 2025, Qi Quan et al. used computational pharmacology, functional experiments, and singlecell RNA sequencing to reveal how Qingdu Zengye Decoction (QZD) treats NPC. They found that QZD induces apoptosis via Bax and inhibits the PI3KAkt pathway. Network pharmacology identified AKT1, MTOR, HIF1A, SRC, and ESR1 as core targets. Singlecell sequencing showed that AKT1/ESR1 are mainly in tumor cells, SRC/IL6 in myeloid cells, and MTOR/HIF1A in stromal cells. Molecular docking confirmed strong binding of QZD’s active components (e.g., quercetin, luteolin) to these targets [6].

3.3 From “ToxinPermeating and RootTonifying” to Efferocytosis: Modern Extension of Theory

The classic TCM summary of NPC pathogenesis is “toxin-stasis-phlegm accumulation with root deficiency and surface excess,” mostly presenting as “heat-toxin congestion with qi-yin deficiency.” In 2025, Tongfei Qi et al., under the “toxin-permeating and root-tonifying” framework, linked TCM theory with the modern concept of efferocytosis. Efferocytosis is the process by which phagocytes clear apoptotic cells. However, in the tumor microenvironment, overactive efferocytosis can impair antigen presentation, restrict immune activation, induce platinum resistance, and promote immune escape. Locally advanced NPC faces low chemotherapy sensitivity and poor long-term survival; a key mechanism is immune silencing caused by excessive efferocytosis. This theory offers a novel, integrated Chinese-Western approach to optimizing treatment for locally advanced NPC[7].

3.4 EvidenceBased Data on Integrated ChineseWestern Medicine

A 2025 systematic review (11 RCTs, 983 patients) evaluated seven TCM injections combined with CCRT for NPC. Results showed that TCM injections significantly increased peripheral blood CD3⁺ and CD4⁺ T cells. Aidi injection was most effective for CD3⁺ (SUCRA 96.50%) and CD4⁺ (96.51%), while matrine injection performed best for CD8⁺ (83.51%) and the CD4⁺/CD8⁺ ratio (82.80%). These immunomodulatory effects may reduce infection risk and enhance tumor immune surveillance [8]. Methodologically, the RCTs could not be blinded due to the nature of TCM injections, but bias risk remained manageable. This reflects the challenge of aligning TCM’s individualized syndrome differentiation with standardized evidencebased paradigms like randomization and blinding. Preserving TCM essence within an evidencebased framework remains an open question.

4. Synergy Between Chinese and Western Medicine: Paradigm Complementarity and Mechanistic Mutual Explanation

4.1 Attenuation of Adverse Effects and Enhancement of Efficacy in Chemoradiotherapy

Side effects of Western medicine limit dose escalation and quality of life. From a TCM perspective, radiotherapy’s

“heattoxin” consumes qi and yin, causing dry mouth, sore throat, and mucositis; chemotherapy damages the spleen and stomach, leading to qiblood deficiency (poor appetite, fatigue, myelosuppression). A 2025 study of 80 NPC patients with qi yin deficiency and heattoxin syndrome after chemoradiotherapy found that adding Yiqi Yangyin Jiedu Fang reduced toxicity and enhanced efficacy. The network metaanalysis further supported TCM adjunctive therapy: TCM injections modulate CD3⁺ and CD4⁺ Tcell subsets, strengthening immune defense alongside Western treatment[8].

4.2 Pathways to Integrative Medicine

Western medicine excels in precise diagnosis, staging, and targeted intervention (e.g., IMRT, immunotherapy) using objective biological indicators. TCM excels in holistic regulation, individualized syndrome differentiation, and multitarget synergy, with active compounds acting on tumor cells, immune cells, and stromal cells to reshape the malignant ecosystem. Integration should not be simply “TCM plus Western drugs,” but mutual calibration under the shared goal of reducing toxicity and enhancing efficacy. TCM’s empirical feedback can optimize individualized Western treatment, while Western precision tools provide quantifiable validation for TCM efficacy.

5. Challenges and Future Directions

Despite progress, NPC research faces challenges in both Western and Chinese medicine. Western challenges: Distant metastasis and local recurrence remain major barriers. Even with IMRT, infield recurrence still occurs – a Heidelberg study of 8 recurrences found 2 in central highdose areas and 3 in marginal highdose areas, indicating room for dose escalation. Moreover, about 30% of highrisk patients develop distant metastasis after standard treatment. TCM challenges: Highquality, largesample, multicenter RCTs are scarce. Standardization of TCM preparations, efficacy evaluation, and seamless integration with Western workflows remain difficult. The individualized nature of TCM syndrome differentiation inherently conflicts with populationbased evidencebased medicine standards. Future directions: Integrate multiomics with TCM syndrome research for biomarkerbased, objective syndrome typing; Develop adaptive trial designs and realworld evidence for flexible TCM validation; Focus on molecular targets of active TCM ingredients in remodeling the tumor immune microenvironment to guide precise intervention timing; Promote standardization and scalability through international multicenter collaboration. NPC research is at a critical stage of transitioning from empirical heritage to evidencebased confirmation and from classical theory to molecular dialogue. The strengths of Eastern and Western medicine will not replace but complement each other, ultimately delivering more precise, safer, and more humane treatment for patients.

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