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Study on Traditional Chinese Medicine Syndrome Types in NPC

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Abstract: As one of head and neck tumors, nasopharyngeal carcinoma (NPC) occurs most frequently in the south of China, especially in Hunan, Guangzhou and other places, causing serious harm to people's life and health. NPC patient is mainly treated with radiotherapy in clinic, but most of them have serious side effects. At present, traditional Chinese medicine (TCM) combined with chemoradiotherapy in the treatment of NPC patient has been focused on by Chinese and Western clinicians. Although TCM syndrome differentiation has significant advantages in the treatment of nasopharyngeal cancer, the relevant syndrome type standards for TCM syndrome differentiation guidance are still not unified. Therefore, this paper summarized the clinical experience, clinical data analysis and experimental research of TCM scholars in recent years, discussed the role and influence of TCM syndrome differentiation on the treatment of NPC. It provides some guidance for the standardization of TCM syndrome differentiation of NPC patients.

Keywords: Nasopharyngeal carcinoma; TCM syndrome type; Syndrome differentiation and treatment; Radiation therapy; Constitution theory

Nasopharyngeal carcinoma (NPC) refers to a malignant tumor originating from the epithelium of the nasopharyngeal mucosa, predominantly occurring in southern China regions such as Hunan, Guangzhou, and Fujian, with its incidence ranking first among head and neck malignancies [1]. Most initially diagnosed NPC patients present at intermediate or advanced stages. Concurrent radiotherapy and chemotherapy serve as effective treatment modalities for these patients; however, the therapeutic regimens are associated with significant side effects, reduced patient tolerance, and high recurrence rates, posing major challenges in clinical management [2]. Currently, traditional Chinese medicine (TCM) demonstrates notable advantages in treating head and neck tumors through mitigating the toxic side effects of radiotherapy and chemotherapy, enhancing patients' immune function, and consequently markedly improving their quality of life [3]. Syndrome differentiation and treatment constitute a distinctive TCM diagnostic and therapeutic approach, serving as the cornerstone for effective tumor management. TCM's syndrome differentiation methodology integrates various theories, including the Eight Principles syndrome differentiation and visceral-meridian syndrome differentiation, to identify the disease site, etiology, and pathogenic relationships, thereby establishing comprehensive syndrome patterns and corresponding therapeutic principles [4]. The essence of TCM syndrome differentiation lies in achieving a holistic understanding of disease pathogenesis, symptoms, and signs to formulate targeted prescriptions addressing primary pathogenic factors. However, standardized TCM syndrome classification criteria for NPC remain inconsistent, with variations in treatment protocols and pharmacological approaches. Moreover, syndrome manifestations at pre- and post-surgical or chemoradiotherapy may vary depending on individual physiological differences, underscoring the critical importance of syndrome differentiation in guiding TCM-based treatment strategies. In recent years, numerous scholars have conducted in-depth investigations into the correlation between TCM syndrome patterns and modern medicine in NPC.

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Pathogenesis of NPC in TCM

There is no specific description of "NPC" in traditional Chinese medical literature. Based on the clinical symptoms described in modern medicine and their correspondence with ancient medical texts, it can be termed as "epistaxis," "nasal abscess," "upper stone carbuncle," "depletion of vital energy," "scrofula," "loss of vitality," "malignant nodule," or "true headache." Shigong Chen of the Ming Dynasty described it in The Authentic Treatise on Surgery [5]: "Over time, the lesion gradually enlarges, becoming hard like stone; it does not move when pushed or pressed. Alternatively, it may swell like a lotus flower, emitting foul odor continuously day and night." Bingjun Gao of the Qing Dynasty noted in Collected Insights on Ulcerology [6], "Similar to a tree losing its vitality..., It arises around the ears and neck, gradually enlarging followed by dull pain, chest tightness, and irritability..." Qian Wu of the Qing Dynasty stated in The Golden Mirror of Medicine [7], "Yellow, turbid nasal discharge flows continuously... If it persists without healing...". Regarding the pathogenesis of NPC, Shigong Chen explained in The Authentic Treatise on Surgery [5] that it results from "the stagnation of stagnant fire, leading to phlegm obstruction and subsequent accumulation"; Collected Insights on Ulcerology [6] attributed it to "depletion of vital energy and drying up of collateral vessels"; Zhang's Medical Compendium [8] described it as "vital energy depletion due to prolonged consumption of expensive foods followed by frugality—even without exposure to pathogens, essential fluids are gradually lost, resulting in internal depletion of vital energy"; while Ma Pei's Surgical Cases [9] linked it to "deficiency of liver and spleen vitality." After reviewing ancient medical literature on NPC, Xiaojun Zhou concluded that the fundamental cause lies in deficiency of vital qi; when this deficiency is compounded by invasion of external pathogens or emotional distress, it further weakens vital qi, ultimately leading to "deficiency of vitality and drying up of collateral vessels" and death [10].

Currently, different scholars of TCM hold varying interpretations regarding the pathogenesis of NPC, but their discussions generally revolve around phlegm, blood stasis, deficiency, and toxicity. Wei Hou [11] posited that the primary pathogenesis of NPC is "yin deficiency with toxin accumulation," where the body lacks nourishment, allowing pathogenic factors to invade. The essence lies in the disruption of the dynamic balance of "yin equilibrium and yang secretion" in the human body; thus, the therapeutic principle should prioritize replenishing qi and nourishing yin, supplemented by clearing heat and resolving phlegm. Xiaojun Zhou et al. [12] concluded that the pathogenesis of NPC involves "failure of Yangming to descend based on the theory of the Five Phases and Six Qi", it means that the failure of Yangming to descend causes fire to rise upward, leading to dryness-heat in the upper jiao. The treatment approach should focus on descending Yangming and tonifying the spleen and stomach. Yueheng Li [13] argued that the fundamental pathogenesis of NPC is "deficiency of the root and excess of the branch", where deficiency of healthy qi serves as the root cause, while phlegm, blood stasis, and toxins interact as the branch manifestations. And this should be addressed differently across stages, patients during chemotherapy, radiotherapy, or/and surgery, exhibit intense heat-toxin accumulation and qi-yin deficiency, requiring that the treatment focuses on tonifying the spleen and replenishing qi. During recovery, patients suffer from dual deficiency of yin and yang, necessitating efforts to restore healthy qi. At post-treatment, the patients occur with coexisting phlegm-blood stasis when disease recurrence or metastasis, the treatment should emphasize softening hard masses and dispersing nodules. Comprehensive analysis of these TCM perspectives revealed that deficiency of healthy qi and generation of internal toxins are pivotal factors in NPC pathogenesis. Dysfunction of visceral organs and qi stagnation with phlegm condensation lead to the accumulation of various pathological products, such as tumor-forming factors, which aligns with classical TCM theories. Professor Daofa Tian [14], drawing on years of clinical experience, posited that most diseases in the human body, including tumors, are closely associated with a qi-deficient constitution from innate constitutional differences. This condition involves an inherent deficiency of the body's vital qi and the endogenous generation of pathogenic toxins. The interaction between these factors leads to progressive depletion of vital qi and the accumulation of internal toxins, producing pathological products such as phlegm and blood stasis, thereby triggering disease onset. This constitutes the fundamental basis of Professor Tian's independently developed "qi-deficiency and toxin accumulation" theory. In this framework, the qi-deficient constitution serves as the root cause of disease; dysfunction of the visceral organs and disruption of yin-yang balance act as internal factors inducing toxin endogenesis, while external exposure to pathogenic toxins constitutes the external factor. The combined impact of these internal and external factors drives the continuous progression of the disease.

Guidelines for TCM Syndrome Types in NPC Patients

Due to regional differences and various understandings among medical practitioners regarding the pathogenesis of NPC, the established TCM syndrome differentiation guidelines have not been standardized, leading to discrepancies in treatment methods and herbal formulations. Moreover, the clinical manifestations of the patients may change after treatments such as radiotherapy, chemotherapy, or surgery. Therefore, the TCM principle of syndrome differentiation and treatment is crucial for guiding the patient management. The 2008" Guidelines for TCM Diagnosis and Treatment of Oncology" [15], issued by the China Association of Chinese Medicine, classified NPC patients into four syndrome patterns: Heat Pathogen Invading the Lungs Syndrome, Liver Stagnation with Phlegm Condensation Syndrome, Blood Stasis Obstructing Collaterals Syndrome, and Qi-Yin Deficiency Syndrome. The guidelines categorize NPC

patients under traditional TCM classifications such as "Nasal Discharge," "Tinnitus Syndrome," "Superior Stone Gangrene," and "Deficiency of Vital Energy." Its primary clinical symptoms include epistaxis, rhinorrhea, tinnitus, and headache, it is accompanied by dry mouth and fever. The core TCM therapeutic principles are: aggressive treatment in the early stage, a combination of aggressive and tonifying therapy in the middle stage, and tonifying therapy in the advanced stage, all guided by the principle of detoxification and collateral dredging. The 2011 edition of "Traditional Chinese Medicine Oncology," edited by Daihan Zhou [16], further classified nasopharyngeal carcnoma into four subtypes: Lung Heat with Phlegm Condensation, Qi Stagnation with Phlegm Stasis, Internal Fire-Toxin Obstruction, and Qi-Yin Deficiency. Zhou emphasized that NPC originates in the nasopharynx, the respiratory tract closely linked to internal organs. The lungs govern qi and open into the nose; internal heat obstruction impairs lung qi circulation, causing nasal congestion and cough; ascending fire transforms fluids into phlegm, resulting in foul-smelling nasal discharge; heat scorches collaterals, forcing blood out of its channels, leading to epistaxis. Concurrent emotional disturbances exacerbate liver qi stagnation and internal fire-toxin obstruction, potentially causing headaches and hearing loss. When phlegm-fire obstructs collaterals and forms masses, cervical phlegm nodules may develop hard as stones and progressively enlarge over time. Therefore, the pathogenesis of NPC is closely related to functional disorders of organs such as the lungs and liver. Clinically, the patients with NPC often present with a mixture of deficiency and excess patterns: nasal obstruction due to impaired lung qi circulation; hemoptysis or epistaxis caused by lung fire scorching the collaterals and forcing blood out of its normal pathways; hearing loss and tinnitus resulting from liver-gallbladder fire stagnation; headache induced by qi rebellion ascending; and neck masses formed by phlegm-stasis and blood stasis. Thus, clinical treatment should differentiate between deficiency and excess patterns, employing therapeutic principles such as clearing heat and toxins to resolving stasis and unblock collaterals, and to replenish qi and nourishing yin [17]. In 2016, the report edited by Tian Daofa [18] classified NPC patients into five syndrome types: qi-blood stasis with blockage at the Hals (pharyngeal region), excessive fire-toxin accumulation causing stagnation at the Hals, dual deficiency of qi and yin with pathogenic stagnation at the Hals, equilibrium between pathogen and healthy qi leading to pathogenic stagnation at the Hals, and qi-yang deficiency with pathogenic toxin dissemination. Through observing tongue manifestations and analyzing constitutional profiles of newly diagnosed NPC patients, Tian et al identified qi deficiency with toxin invasion as the primary TCM pathogenesis. By integrating congenital genetic factor and virulence characteristics of Epstein-Barr virus (EBV) infection, he established a pathogenic axis involving "innate constitution–physical constitution–latent pathogens–new external infections interacting", which holds significant clinical implications for medication guidance in NPC patient management.

TCM Syndrome Differentiation and Classification in NPC Patients

TCM constitution-related syndromes in NPC patients

The incidence of NPC exhibits a gender bias and is influenced by genetic factors, diet, and lifestyle habits [19, 20]. TCM categorizes this comprehensive disease pattern under the framework of TCM constitution theory. In recent years, significant progress has been made in basic research on constitution-related theories and clinical trials involving constitutional regulation interventions for NPC. Variations in patient constitutions exert distinct impacts on TCM diagnosis and treatment; thus, constitution investigations hold substantial scientific significance for the prevention, diagnosis, and management of NPC through TCM approaches.

In 2002, Zhou et al. developed the initial constitution survey questionnaire based on the constitutional clustering analysis results conducted by He et al. They systematically investigated NPC patients and their families according to normal or abnormal constitutions (including weak constitution and dysregulated constitution) [21]. Through multiple regression analysis, they identified weak constitution as a significant risk factor for familial genetic etiology of NPC. Influenced by Tian's theory of "qi deficiency with toxin accumulation", they reclassified weak constitution as qi deficiency constitution, focusing particularly on the progression of cancer driven by qi deficiency [22, 23]. As constitutional advanced studies, a series of classification criteria, including constitutional syndromes, were established with additional composite constitutions such as damp-heat and deficiency-stasis incorporated [24]. Subsequent studies revealed that high-risk NPC populations predominantly exhibited qi deficiency constitution; most NPC patients displayed dysregulated constitution; and post-radiotherapy cases often exhibited composite constitutions involving qi deficiency mixed with phlegm, heat, and dampness, demonstrating that constitutional changes permeate the entire course of NPC development [25]. The clinical study on NPC patient constitutional syndrome scores found that qi deficiency constitution predominates among precancerous lesions, while composite constitutions were more common in post-treatment patients [26]. This classification aligns well with the constitutional characteristics of the Lingnan population, where qi deficiency constitution ranked highest in traditional Chinese medicine constitution scales [27], indicating that NPC constitutional classification reflects disease progression patterns and exhibits regional correlations with affected populations.

Epstein-Barr virus (EBV) exhibits a close association with NPC. Epidemiological analyses of the constitution of EBV-infected individuals revealed that EBV-positive populations predominantly exhibit a qi-deficient constitution. Upon EBV invasion, the immune system promptly activates to eliminate the virus, manifesting as symptoms such as fever and sore throat due to the interaction between pathogenic and healthy qi. In cases of compromised or impaired

immune function, EBV may remain latent within the body, presenting as EBV infection, a condition where TCM characterizes the constitution as qi-deficient. Without proper regulation, this may progress NPC. The entire process of EBV latency leading to carcinogenesis aligns closely with the TCM principle of "deficiency harboring pathogenic factors" [28]. Yang et al., through analysis of the constitution of EBV-positive individuals, identified qi-deficient and yang-deficient constitutions as the predominant patterns among these patients, and they applied constitutional intervention therapy to the early management of NPC patients [29].

The constitutional theory of NPC exhibits a certain correlation with genetic factors. With science and technology development, fundamental investigation on this theory has become increasingly robust. Some studies have revealed significant proteomic differences among individuals with distinct constitutions in NPC [30]. Notably, microRNA profiles differ markedly between patients with qi-deficient constitution and those without qi-deficient constitution, with the former exhibiting a promoting effect on malignant behavior of cancer cells [31]. He et al. employed gene recombination technology to construct a dual-gene eukaryotic expression vector targeting human p53 protein and EBV latent membrane protein 1 for investigating the qi-deficient constitution in NPC. Animal experiments demonstrated that, compared to the control group, 117 genes in the nasopharyngeal epithelium of the rats with qi-deficient constitution exhibited differential expression, including interleukin-1β and glutathione synthase [32]. Cheng et al. induced rat with qi-deficient constitution NPC using dinitrophenylpiperazine (DNP), finding a significantly higher incidence of cancer cases in the qi-deficient group compared to the DNP-only induction group, indicating a close association between NPC development and the qi-deficient constitution [33].

Evolutionary patterns of TCM syndrome types in patients with NPC undergoing radiotherapy and chemotherapy

Currently, due to the significant divergence between modern lifestyles and dietary patterns from those described in ancient Chinese medical texts, the diagnosis and treatment of this disease require not only reliance on the experience of traditional physicians but also integration with modern medical technologies. Modern clinicians advocate that the pathogenesis of NPC under TCM should be analyzed in conjunction with different stages of radiotherapy and chemotherapy. Wu et al. [34, 35] posited that the pathogenic mechanism of NPC involves carcinogenic toxins, deficiency of vital qi, progressive impairment of vital qi following multiple radiotherapy sessions, with dual deficiency of qi and yin as the root cause and the interplay of phlegm, stasis, and toxins as the clinical manifestation; thus, treatment should prioritize nourishing yin and clearing heat while addressing liver and kidney function, along with anticancer and detoxification therapies. Xu et al. [36] emphasize that early-stage NPC management should focus on eliminating pathogens through medications that resolve phlegm, dissipate masses, remove stasis, and clear heat, whereas advanced-stage treatment should prioritize reinforcing vital qi, with the therapeutic key lying in "regulating qi and blood circulation and balancing yin and yang" through using herbs to tonify lung yin and nourish kidney fluids. Sun et al. [37] identified the core pathogenesis as initial deficiency of vital qi followed by accumulation of phlegm-heat, internal obstruction by toxic heat, and subsequent tumor formation. Post-radiotherapy complications primarily warrant treatment principles centered on "clearing heat and promoting fluid production." Currently, radiotherapy remains the primary treatment for NPC patients, often accompanied by vital qi deficiency and spleen-kidney impairment. He et al. [38] asserted that spleen-kidney deficiency constitutes the fundamental etiology of NPC, with clinical and pathological manifestations predominantly including heat-toxin and blood stasis. Li et al. [39] contended that post-radiotherapy complications such as throat dryness are closely associated with spleen-stomach dysfunction, rooted in yin deficiency and accompanied by symptoms of heat-toxin, phlegm-turbidity, and blood stasis. Chen et al. [40] posited that the toxic and adverse reactions in NPC patients after radiotherapy are attributed to pathogenic mechanisms involving excessive heat-toxin, yin deficiency with dryness-heat, spleen-stomach qi deficiency, and latent pathogenic factors. Treatment should focus on reinforcing healthy qi, eliminating pathogens, promoting fluid production, and replenishing qi. Lin et al. [41, 42], from a TCM meridian perspective, analyzed that NPC involves the liver and lung organs, with its primary pathogenesis being pathogenic heat invading the lungs and liver qi stagnation leading to phlegm coagulation. Therapeutic approaches should emphasize lung ventilation to clear heat and nourishing the liver and kidneys. Huang et al employed systematic cluster analysis to investigate the patterns of TCM syndrome changes in NPC patients at pre- and post- chemoradiotherapy, revealing that these syndromes undergo continuous evolution from predominantly excess patterns to deficiency patterns or mixed patterns, while emphasizing that both chemoradiotherapy and radiotherapy introduce "toxic pathogens" that exacerbate systemic "deficiency, toxicity, and blood stasis" [43]. Pan et al. suggested that post-chemoradiotherapy patients typically present with dual qi-yin deficiency and internal blood stasis-toxicity accumulation, advocating treatments aimed at replenishing qi and yin while resolving stasis and dispersing nodules [44]. Chen et al. concluded that post-chemoradiotherapy manifestations primarily involve dual qi-blood deficiency, necessitating "dual supplementation of qi and yin" as the therapeutic principle [45]. These studies collectively indicate that the core pathogenesis of NPC involves fundamental deficiency with superficial excess and impaired healthy qi. Post-treatment, patients often experience qi depletion and fluid loss, compounded by upper-jiao dryness-heat and middle-jiao deficiency-cold, resulting in complex pathological mechanisms characterized by concurrent cold-heat manifestations, such

as phlegm-heat interaction and phlegm-dampness stagnation.

Correlation between pathological staging and TCM syndrome differentiation in NPC patients

Zhang et al. found that in NPC patients, as the TNM pathological stage advanced, the syndrome patterns evolved from "fire-toxin stagnation type" to "qi deficiency congealing type", and further to "deficiency of healthy qi with toxin retention type" [46]. Li et al. observed that, with increasing pathological stages, the syndrome patterns progressed from "pathogenic heat obstructing the lungs type" to "phlegm-turbidity accumulation type," and then to "blood stasis with phlegm coagulation type" [47]. Zhou et al. demonstrated a negative correlation between pathological stages and the lung-heat predominance type or qi stagnation with phlegm coagulation type, while showing a positive correlation with blood stasis obstructing collaterals type or yin deficiency with fire hyperactivity type [48]. These findings indicate that phlegm, blood stasis, and heat are consistently present throughout all pathological stages of NPC; the lung-heat pattern is predominantly observed in early-stage cases, whereas intermediate and advanced-stage patients typically exhibit deficiency of healthy qi accompanied by mutual entanglement of phlegm and blood stasis.

Correlation between prognostic indicators and TCM syndrome differentiation types in NPC patients

The study found that serum C-reactive protein (CRP) levels exhibit a certain correlation with the TCM syndrome differentiation patterns in newly diagnosed NPC patients. Specifically, CRP levels from low to high correspond to the following patterns: heat pathogen invading the lungs type, liver qi stagnation with phlegm obstruction type, dual deficiency of qi and yin type, and blood stasis obstructing collaterals type [49]. Gao et al. observed that, among patients with different TCM syndrome types, those with blood stasis obstructing collaterals type exhibited higher serum TGF-β1 expression levels, suggesting a potential association with poorer prognosis [50]. Li et al. reported that newly diagnosed NPC patients predominantly presented with phlegm-turbidity accumulation syndrome or qi-blood stasis syndrome. The patients with qi-blood stasis syndrome showed higher serum EGFR levels compared to other syndrome types, leading to the conclusion that their prognosis may be worse [51]. Yan et al. found that the patients with phlegm-turbidity accumulation syndrome or deficiency with toxic stagnation syndrome exhibited higher EGFR expression levels in NPC tissues than those with qi-blood stasis syndrome or fire-toxicity accumulation syndrome, indicating potentially poorer prognosis for these groups [52]. Li et al. demonstrated that patients with phlegm-turbidity internal obstruction syndrome had higher VEGF expression in tumor tissues, while post-radiotherapy/chemotherapy patients with phlegm-stasis and qi stagnation syndrome exhibited the highest VEGF levels in tumor tissues [53].

TCM syndrome differentiation and typing therapy for NPC

There is no unified standard for the TCM syndrome differentiation and classification of NPC patients. Based on previous reports, the patterns can be summarized as follows: Lung Heat Excess Pattern (with the primary treatment principle being lung ventilation and heat clearance), Liver Stagnation with Phlegm Condensation Pattern (with the main therapeutic approach being liver regulation and depression relief), Qi Stagnation with Blood Stasis Pattern (with key treatments including liver regulation, qi circulation improvement, stasis resolution, and nodule dispersion), Qi-Yin Deficiency Pattern (with emphasis on qi replenishment and yin nourishment), and Qi-Blood Deficiency Pattern (with focus on qi and blood supplementation). Guo et al. posited that NPC patients exhibited deficiency of vital qi, with prolonged accumulation of pathogenic toxins leading to cancer development. Therefore, the therapeutic principle should emphasize heat-clearing, yin-nourishing, and fluid generation, often employing herbs such as honeysuckle (Lonicera japonica) and forsythia (Forsythia suspensa) for heat-clearing and detoxification [54]. Jia et al. argueed that post-radiotherapy NPC patients resembled those with warm-heat syndromes, thus frequently prescribing Wuwei Xiaodu Decoction combined with Yangyin Qingfei Decoction to tonify lung qi, achieving excellent efficacy [55]. Based on extensive clinical experience, Zhang et al identified that advanced-stage NPC most commonly presents dual qi-yin deficiency, particularly in the patients treated with radiotherapy and chemotherapy. Consequently, late-stage patients often receive herbs such as Rehmanniae Radix (Shengdi), Pseudostellariae Radix (Taizi Shen), Scrophulariae Radix (Yuanshen), and Hedyotis diffusa (Baihua Shecao) for their heat-clearing, detoxifying, yin-nourishing, and fluid-promoting properties [56]. Tian et al. developed a qi-tonifying and detoxifying formula grounded in the "qi deficiency with toxin accumulation" theory, demonstrating remarkable therapeutic efficacy in treating NPC patients [57]. The study found that the Yiqi Jiedu Formula can induce autophagy in NPC cells by inhibiting the PI3K/AKT/mTOR signaling pathway [58]; suppress NPC cell proliferation by downregulating the Wnt/β-catenin signaling pathway [59]; and regulate the proliferation, migration, and apoptosis of NPC stem cells by inhibiting the CD44/Ras signaling pathway [60]. Zou et al. employed network pharmacology and bioinformatics techniques to demonstrate that the Yiqi Jiedu Formula may treat NPC through signaling pathways such as TNF and NF-κB [61]. These findings highlight the significant advantages of TCM syndrome differentiation in treating NPC, where tailored medication based on distinct TCM syndromes helps stabilize tumor growth, enhance patients 'immune function, mitigate the toxic side effects of radiotherapy and chemotherapy, alleviate clinical symptoms, and improve patients' quality of life.

Summary and Prospects

Differential diagnosis and treatment constitute the core of TCM. Accurate "differential diagnosis" guiding appropriate "treatment" is a critical guarantee for achieving optimal clinical efficacy. The disease names used in ancient TCM texts primarily reflect specific symptoms, differing from those in modern medicine, leading to the phenomenon of multiple disease names for a single condition. Although advancements in technology have expanded human understanding of diseases, the traditional TCM diagnostic approach relies predominantly on clinicians' experience in assessing disease patterns, resulting in a lack of objectivity in TCM differential diagnosis. Currently, there is no unified standard for TCM differential diagnosis criteria for NPC patients, and different practitioners derive varying conclusions and recommendations based on their clinical experience and investigation. In recent years, the application of big data statistical analysis to clinical data, including retrospective and prospective studies, has gradually reduced variations in TCM clinical practice caused by geographical or dietary factors, thereby providing a more objective and accurate representation of TCM syndrome types for NPC. This offers essential evidence for standardizing TCM syndrome classification. Particularly, noteworthy are studies on TCM differential typing after radiotherapy and chemotherapy; following "precise differential diagnosis" and "targeted treatment", these approaches can effectively mitigate the toxic side effects induced by chemoradiotherapy. The patients with NPC may exhibit varying clinical manifestations due to differences in constitution, clinical-pathological stages, age, and gender. However, the correlation between these influencing factors and TCM syndrome differentiation remains unclear in existing studies. Currently, TCM syndrome differentiation of NPC at post- radiotherapy and chemotherapy is predominantly based on clinicians' empirical judgment, lacking objective data support, a potential contributing factor to the significant variability in TCM syndrome outcomes. Future study should integrate comprehensive patient data, including clinical stage, tumor size and location, pre-and post-treatment parameters, specific chemoradiotherapy regimens, and imaging findings, to investigate correlations. Such efforts will enhance the practical application of TCM syndrome differentiation in clinical practice, and provide robust evidence for the effective use of TCM in NPC treatment.

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