

Targeted Therapy for Nasopharyngeal Carcinoma and Long-Term Nursing Care After Radiotherapy: A Review

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Abstract. Nasopharyngeal carcinoma (NPC) is a common head and neck malignancy for which radiotherapy remains the main curative treatment. In practice, however, tumor recurrence, distant metastasis, and late radiation injury still limit long-term outcomes. With the development of molecular therapy, EGFR-targeted agents are increasingly used together with chemoradiotherapy in selected patients with locally advanced NPC. This combined strategy may improve tumor control, but it also makes symptom management more complicated. Oral mucositis, radiation dermatitis, dysphagia, xerostomia, and skin toxicities may persist beyond the treatment period and directly affect nutrition, communication, social activity, and quality of life. From a nursing perspective, these problems cannot be managed only during hospitalization. This review discusses the clinical value of targeted therapy in NPC and summarizes long-term nursing care after radiotherapy, including complication management, psychosocial support, and transitional care. Available evidence suggests that EGFR-targeted therapy may be useful for appropriate patients, while continuous and specialized nursing care is essential for maintaining treatment adherence and improving recovery.

Keywords: nasopharyngeal carcinoma, targeted therapy, cetuximab, radiotherapy, long-term nursing care

1. Introduction

Nasopharyngeal carcinoma arises from the nasopharyngeal epithelium and is closely related to Epstein-Barr virus infection, genetic susceptibility, and environmental exposure. Because the primary lesion is hidden and early symptoms are often nonspecific, many patients are diagnosed only after the disease has reached a locally advanced stage. Radiotherapy, especially intensity-modulated radiotherapy (IMRT), has improved local control, but recurrence and metastasis remain clinically important. At the same time, late complications such as radiation-induced xerostomia, trismus, and temporal lobe necrosis may continue for years and seriously reduce quality of life [1].

Targeted therapy and immunotherapy have gradually become important additions to NPC treatment. EGFR-targeted agents, represented by cetuximab and nimotuzumab, inhibit downstream signaling by binding to EGFR, thereby suppressing cell proliferation and promoting apoptosis. Clinical studies have reported benefits in locally advanced and recurrent/metastatic NPC [2]. In addition, PD-1/PD-L1 inhibitors have changed the treatment landscape for recurrent or metastatic

disease. The JUPITER-02 trial showed that toripalimab plus chemotherapy prolonged progression-free survival [3], and CAPTAIN-1st reported a similar advantage for camrelizumab [4]. These therapies have also been reflected in recent clinical guidelines [5]. Their use, however, is accompanied by new adverse effects, including acneiform rash, xerosis cutis, paronychia, immune-related dermatitis, thyroid dysfunction, and pneumonitis, all of which increase the burden of clinical monitoring [6].

Most existing reviews emphasize antitumor efficacy, molecular mechanisms, or drug combinations. By contrast, the nursing consequences of these new treatment patterns have received less systematic attention. Patients treated with radiotherapy plus targeted or immune agents may experience overlapping symptom clusters: traditional radiation injury, dermatologic toxicity, mucosal inflammation, nutritional problems, and emotional distress often occur together rather than separately [7]. In this setting, nurses are not only responsible for routine care; they also monitor adverse effects, guide rehabilitation, identify psychological risk, and coordinate follow-up within the multidisciplinary team. A nursing-oriented synthesis is therefore needed to connect oncological treatment with long-term recovery.

This review aims to summarize the efficacy and safety profile of targeted therapy in NPC, organize practical nursing strategies for long-term complications after radiotherapy, and discuss a patient-centered follow-up model that may be used in clinical nursing practice.

2. Clinical efficacy of targeted therapy for NPC

2.1. Classification and mechanisms of EGFR monoclonal antibodies

EGFR monoclonal antibodies, especially cetuximab and nimotuzumab, are the most frequently discussed targeted agents in NPC. EGFR is often overexpressed in NPC tissues, and its activation can promote proliferation, angiogenesis, invasion, and radioresistance through pathways such as RAS-RAF-MEK-ERK and PI3K-AKT-mTOR [8]. Cetuximab is a chimeric IgG1 antibody. It blocks ligand-induced receptor phosphorylation and may also induce antibody-dependent cell-mediated cytotoxicity. Nimotuzumab is more humanized and is generally associated with lower immunogenicity and fewer infusion-related reactions [9]. EGFR tyrosine kinase inhibitors, including gefitinib and apatinib, have also been explored, mainly in recurrent or metastatic NPC [6].

Although cetuximab and nimotuzumab act on the same receptor, their clinical profiles are not identical. A network meta-analysis suggested that nimotuzumab may have advantages in complete response and overall response for primary tumors, although no clear difference in 1- and 2-year overall survival was observed. Cetuximab was linked to higher rates of acneiform rash and mucositis [9]. For recurrent or metastatic disease, meta-analytic evidence also indicates that EGFR-targeted therapy combined with chemotherapy may improve response in some patients, but the quality and consistency of evidence remain limited [10]. At present, EGFR gene amplification, mutation status, and related biomarkers are still insufficiently validated for routine patient selection.

2.2. Targeted therapy in locally advanced NPC

For locally advanced NPC, adding EGFR monoclonal antibodies to chemoradiotherapy has been investigated as a way to strengthen tumor control. In a retrospective cohort of 1,628 patients with stage II-IVb NPC, cetuximab or nimotuzumab combined with concurrent chemoradiotherapy achieved a 3-year overall survival rate of 96.6%, compared with 92.9% in the chemoradiotherapy-alone group ($P=0.015$). The corresponding 3-year progression-free survival rates were 93.5% and

86.9% ($P=0.028$) [1]. Another propensity score-matched study comparing EGFR monoclonal antibodies plus IMRT with cisplatin-based IMRT found no significant difference in PFS, locoregional control, or OS, suggesting that EGFR monoclonal antibodies may be considered mainly when cisplatin is poorly tolerated [2]. More recent reviews continue to support the biological rationale for combining radiotherapy with targeted therapy, especially through radiosensitization and possible reduction of distant metastasis [11].

These findings should be interpreted cautiously. Much of the available evidence is retrospective, and patient selection may affect the observed survival advantage. Large prospective randomized trials have not yet proven that EGFR monoclonal antibodies are superior to standard cisplatin-based regimens. Therefore, cisplatin-based chemoradiotherapy remains the standard approach in current practice, while EGFR monoclonal antibodies are more often positioned as alternatives or supplements for selected patients, particularly those who cannot tolerate cisplatin-related toxicity.

2.3. Adverse effect profiles

When EGFR monoclonal antibodies are combined with radiotherapy or chemotherapy, adverse effects can no longer be understood as isolated drug reactions. They usually include both targeted therapy-specific toxicities and radiation-related injuries, and these problems often overlap during the same treatment period. Recent reviews have emphasized that such combined toxicities require integrated assessment and nursing management [11, 12].

The most typical targeted therapy-related toxicities are dermatologic. Acneiform rash, xerosis cutis, pruritus, and paronychia are commonly observed. Severe rash (grade ≥ 3) has been reported in about 15%-25% of patients treated with cetuximab, often appearing within the first one to two weeks after treatment begins [2]. Nimotuzumab generally causes fewer skin reactions. Infusion-related reactions may also occur, presenting as fever, chills, rash, or dyspnea; in severe cases, emergency management for anaphylaxis may be required.

Radiotherapy adds another layer of toxicity. Acute reactions include oral mucositis, radiation dermatitis, and odynophagia, while long-term complications include xerostomia, trismus, radiation caries, and temporal lobe necrosis. Once EGFR monoclonal antibodies are added to radiotherapy, mucositis and dermatitis may become more severe. One study reported grade ≥ 3 oral mucositis in approximately 35%-40% of patients receiving combined treatment [2].

For nurses, the practical task is to identify these toxicities early and keep them from interrupting treatment. Standardized grading with CTCAE criteria, preventive skin care, stepwise rash management, oral mucosa protection, pain control, and timely nutritional support should be incorporated into routine care rather than handled only after symptoms become severe.

3. Long-term nursing strategies after radiotherapy

Long-term nursing after radiotherapy should be regarded as a continuous process that links hospital, community, and home care. It is not enough to give patients several discharge instructions and wait for the next outpatient visit. As treatment becomes more complex, symptom burden also expands: patients may face radiation injury, residual targeted therapy-related toxicities, nutritional difficulty, and psychological distress at the same time. A more workable framework should start with risk assessment before treatment, continue with monitoring during treatment, and extend to structured follow-up after discharge. The following section is organized around assessment, stratified intervention, monitoring, and dynamic adjustment.

3.1. Stratified nursing for long-term radiotherapy complications

3.1.1. Oral care

Radiation-induced xerostomia and caries are among the most common late complications. Salivary gland fibrosis is often most obvious within 6-12 months after radiotherapy. Nursing care should include regular oral assessment every 3-6 months, including caries risk and salivary flow; daily oral hygiene with fluoride toothpaste and a soft-bristled toothbrush; symptom relief with artificial saliva spray and saline rinses; and professional fluoride application every 6-12 months when possible. If dry mouth seriously affects eating or speaking, patients should be referred for salivary substitutes or sialogogues.

3.1.2. Swallowing function rehabilitation

Dysphagia directly affects food intake, nutritional status, and social interaction. Swallowing assessment should therefore become part of routine follow-up rather than an occasional response to patient complaints. Screening may be arranged at 1, 3, and 6 months after radiotherapy and then every 6 months. Patients with abnormal screening results should receive videofluoroscopic or fiberoptic assessment to clarify the type and severity of dysfunction.

Rehabilitation training needs to be individualized. Common exercises include the Mendelsohn maneuver to maintain laryngeal elevation, effortful swallowing to strengthen tongue base and pharyngeal contraction, and the Shaker exercise to improve hyolaryngeal movement. Compensatory strategies such as chin-tuck positioning, food consistency modification, and bite-size control may also be useful. In daily care, adherence is often the real difficulty. A rehabilitation diary checked regularly by nurses can make training more visible and easier to adjust.

3.1.3. Trismus management

Trismus is mainly caused by radiation-induced fibrosis of the masticatory muscles and temporomandibular joint. It may continue to progress from 6 months to 2 years after radiotherapy, so preventive training should begin early rather than after mouth opening has already become severely restricted.

Maximum interincisal distance (MID) is a simple and useful follow-up indicator. A normal value is about 35-45 mm; 25-34 mm may be considered mild restriction, 15-24 mm moderate restriction, and <15 mm severe restriction. Training can be stratified according to MID: patients with MID ≥ 30 mm may perform active exercises two to three times daily; those with MID 15-29 mm may need active-passive training with a device; and patients with MID <15 mm and obvious pain should begin with heat therapy and massage before gradual stretching. Pain should be recorded using the Numeric Rating Scale, and exercises should be paused when pain reaches 5 or higher.

3.1.4. Early recognition of radiation-induced brain injury

Radiation-induced brain injury is less common than oral or swallowing complications, but it is one of the most serious late injuries. Reported incidence ranges from 0.9% to 4.0%, and the damage may be irreversible [13]. Patients receiving doses above 70 Gy, those undergoing re-irradiation, and patients with vascular comorbidities require closer observation. Neurological screening every 6 months is advisable, together with objective cognitive assessment such as MMSE or MoCA. If headache, memory decline, personality change, seizures, or other suspicious symptoms appear, brain

MRI should be arranged promptly. Baseline assessment is particularly important because cognitive changes are often most active within the first 1-2 years after radiotherapy.

3.2. Psychosocial support

Psychosocial problems after radiotherapy are common but easily underestimated. Patients may feel embarrassed by changes in speech, facial appearance, eating ability, or oral dryness, and these problems can reduce social participation [7]. Nursing support should follow a screening-assessment-intervention pathway. HADS or PHQ-9 may be used at 1 and 6 months after radiotherapy and then annually. When screening is positive, nurses should conduct further interviews to distinguish temporary emotional fluctuation from clinically significant distress. Mild distress may be managed through explanation, empathetic listening, and family support, while moderate or severe distress should prompt referral for cognitive-behavioral therapy or medical treatment. A randomized trial showed that cognitive-behavioral and psychological interventions improved quality of life, resilience, and hope among NPC patients receiving radiotherapy [14].

3.3. Transitional care model

Transitional care is intended to carry professional support into the home and community. Evidence on symptom clusters shows that discharged NPC patients may experience eating-related pain, social difficulty, psychological distress, stigma, throat injury, and sensory abnormalities [7]. These symptoms often reinforce one another; for example, swallowing pain may reduce eating, poor nutrition may delay recovery, and social avoidance may worsen anxiety. Nursing plans should therefore address symptom clusters rather than one complaint at a time.

A practical follow-up schedule may include visits every 3 months in the first year, every 6 months in the second year, and annually from the third year onward. Each follow-up should cover physical symptoms, functional recovery, nutrition, and psychological status. Studies on self-care combined with predictive nursing have reported better quality of life and lower anxiety and depression scores than routine care [15]. Earlier nursing reports on radiotherapy combined with molecular targeted drugs also suggest that structured nursing intervention may improve treatment tolerance and symptom control [16, 17]. Mobile health platforms, including symptom diaries, rehabilitation videos, and remote alerts, may further improve transitional care efficiency [15].

4. Discussion and future directions

4.1. The value of targeted therapy and nursing challenges

Current evidence indicates that EGFR-targeted agents combined with chemoradiotherapy may benefit selected patients with locally advanced or recurrent/metastatic NPC. Cetuximab and nimotuzumab appear broadly comparable in long-term survival, but nimotuzumab has a more favorable safety profile, especially regarding rash and mucositis. This difference is clinically meaningful for nurses because skin and mucosal reactions are not minor discomforts; they may affect nutrition, sleep, treatment adherence, and willingness to continue therapy. Recent reviews also note that targeted therapy and immunotherapy are reshaping NPC treatment while creating new demands for adverse effect monitoring [12].

The value of targeted therapy should therefore be judged together with its symptom burden. In addition to survival and tumor response, treatment-related quality of life, patient-reported

symptoms, adverse effect tolerability, and rehabilitation outcomes should be included in evaluation. Nursing care can contribute by preventing skin injury, managing rash step by step, controlling mucositis, supporting nutrition, and recognizing psychological distress early. These outcomes are still underreported in many clinical studies, which makes it difficult to fully evaluate the nursing contribution.

4.2. Current gaps in long-term nursing care

Several gaps still prevent treatment success from becoming rehabilitation success. First, long-term nursing protocols remain inconsistent across institutions, especially in follow-up frequency, assessment tools, and timing of intervention. Second, psychosocial support is often weaker than physical symptom management, even though cognitive-behavioral interventions have shown benefit. Third, nursing-sensitive outcomes, such as functional recovery trajectory, self-care ability, adherence to rehabilitation, and self-efficacy, are not yet routinely measured. Fourth, community and home nursing resources are limited, so many patients lose professional guidance after discharge.

4.3. Future directions

Future work should proceed at clinical, technological, and research levels. Clinically, unified risk assessment after radiotherapy is needed to guide individualized follow-up. Patients with higher risk, such as those receiving more than 70 Gy, patients with diabetes, or older adults, should receive closer observation, while low-risk patients may follow a less intensive schedule. At the technology level, mobile applications that include symptom diaries, rehabilitation videos, medication reminders, and warning alerts could reduce the pressure on specialist nurses. At the research level, more attention should be given to validating nursing interventions, building nursing-sensitive outcome indicators, and conducting multicenter long-term follow-up studies.

5. Conclusion

This review summarizes targeted therapy for NPC and long-term nursing care after radiotherapy. EGFR-targeted agents combined with radiotherapy or chemotherapy may improve outcomes for selected patients with locally advanced or recurrent/metastatic disease, but their use also increases the complexity of adverse effect management. Systematic long-term nursing care is therefore necessary for treatment safety and quality-of-life improvement. Key priorities include prevention and rehabilitation of late radiation injury, management of skin and mucosal toxicities, psychological support, and transitional care that links hospital, community, and home. Future work should focus on standardized nursing protocols, stronger psychosocial support, and feasible remote nursing models for long-term follow-up.

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