# PRELIMINARY EVALUATION OF CONCURRENT CHEMORADIOTHERAPY USING IMRT COMBINED WITH LOW-DOSE CISPLATIN FOR STAGE II–IVA NASOPHARYNGEAL CARCINOMA AT MILITARY HOSPITAL 175

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## ABSTRACT

***Objective:*** *To determine the response rates at 3 and 6 months of concurrent chemoradiotherapy using intensity-modulated radiation therapy (IMRT) combined with low-dose cisplatin in patients with stage II–IVA nasopharyngeal carcinoma (NPC) and to evaluate treatment-related toxicities.*

***Subjects and Methods:*** *A total of 93 patients with stage II–IVA nasopharyngeal carcinoma underwent concurrent chemoradiotherapy using IMRT combined with weekly low-dose cisplatin. This was a descriptive, retrospective study. Data were collected at 3 and 6 months following completion of treatment. The study was conducted from August 2024 to August 2025.*

***Results:*** *The mean age of the study population was 49.17 ± 25.26 years. The proportions of patients with stage II, III, and IVA disease were 15.1%, 32.3%, and 52.7%, respectively. The distribution of primary tumor (T) stage was T1, T2, T3, and T4 in 14.0%, 25.8%, 28.0%, and 32.2% of patients, respectively. Nodal (N) stage distribution was N0, N1, N2, and N3 in 18.3%, 23.7%, 30.1%, and 27.9% of cases, respectively. Most patients had World Health Organization (WHO) type II and III histopathology (94.6%). At the 6-month evaluation, the complete response (CR) rates for overall disease, primary*

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*tumor, and nodal disease were 87.1%, 92.4%, and 95.6%, respectively. Several factors were associated with treatment response: patients with stage IVA disease, T4 tumors, or N3 nodal involvement had lower CR rates compared with earlier stages. Patients with WHO type III histology, who completed the full chemotherapy regimen, and who did not experience treatment interruption had higher CR rates. Most treatment-related toxicities were mild and had minimal impact on treatment compliance. The rates of grade 3 leukopenia and anemia were 15.7% and 4.3%, respectively. The incidences of grade 3 dermatitis, mucositis, and xerostomia were 15.1%, 30.1%, and 8.6%, respectively.*

***Conclusion:*** *Concurrent chemoradiotherapy using IMRT combined with low-dose cisplatin in stage II–IVA nasopharyngeal carcinoma patients achieves a high complete response rate with manageable toxicity. It remains the current standard of care.*

***Keywords:*** *Nasopharyngeal carcinoma; concurrent chemoradiotherapy; IMRT; low-dose cisplatin.*

## 1. INTRODUCTION

According to GLOBOCAN 2022 data, nasopharyngeal carcinoma (NPC) is the third most common head and neck cancer worldwide. In Vietnam, NPC ranks first in incidence and mortality among head and neck cancers. Radiotherapy is the most important treatment modality for NPC. Currently, advanced radiotherapy techniques such as IMRT and VMAT are considered the standard of care in NPC treatment [1,2]. Additionally, combining concurrent cisplatin chemotherapy with radiotherapy has been shown to improve treatment efficacy and is indicated for patients with stage II or higher, particularly stage III–IVA disease. At Military Hospital 175, concurrent chemoradiotherapy using IMRT combined with low-dose cisplatin has been implemented for NPC patients since 2020; however, outcomes of this regimen have not been systematically evaluated. Therefore, we conducted this study with two objectives:

*1. Determine the response rates at 3 months and 6 months after concurrent chemoradiotherapy.*

*2. Evaluate selected toxicities of the treatment regimen.*

## 2. SUBJECTS AND METHODS

### Study subjects

This study included patients with nasopharyngeal carcinoma who underwent concurrent chemoradiotherapy at the Oncology and Nuclear Medicine Center of 175 Military Hospital from January 2020 to December 2023.

Inclusion criteria: patients aged ≥18 years with performance status (PS) 0–1; histopathology classified as WHO type I, II, or III (2005 WHO classification); disease stage II, III, or IVA according to AJCC 8th edition (2017); treated with IMRT and weekly low-dose cisplatin chemotherapy.

Exclusion criteria: inadequate liver or kidney function or abnormal electrolyte levels precluding concurrent chemoradiotherapy; prior radiotherapy to the head and neck region; medical records lacking sufficient data for the study.

**Study methods**

This was a descriptive, retrospective study. Data were collected using a standardized case report form and entered using Epidata software. Statistical analysis was performed with R software. Binary logistic regression was applied using a backward stepwise likelihood ratio method. The Hosmer–Lemeshow test was used to assess model fit. Results were considered statistically significant at $p < 0.05$.

## 3. RESULTS

### 3.1. Patient characteristics

A total of 93 patients met the inclusion criteria. The mean age was 49.17 ± 25.26 years.

**Table 1. Clinical characteristics of patients (n = 93).**

| Characteristic | Result |
|---|---|
| Disease stage | |
| Stage II | 15.1% |
| Stage III | 32.3% |
| Stage IVA | 52.7% |
| T stage | |
| T1 | 14.0% |
| T2 | 25.8% |
| T3 | 28.0% |
| T4 | 32.2% |
| N stage | |
| N0 | 18.3% |

| | |
|---|---|
| N1 | 23.7% |
| N2 | 30.1% |
| N3 | 27.9% |
| Largest nodal size | |
| None (no nodal involvement) | 19.4% |
| ≤ 6 cm | 73.1% |
| > 6 cm | 7.5% |
| Extranodal extension (ENE) | |
| Yes | 17.1% |
| No | 82.9% |

### 3.2. Treatment response

**Table 2. Complete response rates at 3 and 6 months.**

| Timepoint | CR – Overall | CR – Primary tumor | CR – Lymph nodes |
|---|---|---|---|
| 3 months | 89.2% | 92.4% | 96.7% |
| 6 months | 87.1% | 92.4% | 95.6% |

Table 2 shows complete response (CR) rates at 3 and 6 months after treatment. At the 6-month evaluation, most patients achieved complete response (87.1%). Four patients (4.3%) had partial response. Treatment failure occurred in 8.6% of patients, including 3 patients with locoregional progression and 5 patients with distant metastases (3 to the lungs, 1 to bone, and 1 to the liver).

### 3.3. Factors associated with response

Table 3 presents factors influencing complete response. In multivariate logistic regression, stage IVA (vs II–III), T4 (vs T1–3), N3 (vs N0–2), WHO type II histology (vs type III), receiving <5 cisplatin cycles, and treatment delay >7 days were independently associated with a lower likelihood of complete response (adjusted $p < 0.05$ for each).

**Table 3. Factors affecting complete response rate.**

| Factor | CR (%) | OR (unadjusted) | 95% CI | p (univariate) | aOR | 95% CI | p (multivariate) |
|---|---|---|---|---|---|---|---|
| Age < 60 vs ≥ 60 | 84.2 vs 87.0 | 0.82 | 0.31–2.13 | 0.74 | | | |
| Sex (Male vs Female) | 88.6 vs 71.4 | 2.97 | 0.61–14.5 | 0.20 | | | |
| Comorbidity (No vs Yes) | 85.7 vs 86.0 | 0.98 | 0.34–2.84 | 1.00 | | | |
| Stage (II–III vs IVA) | 100.0 vs 73.5 | 4.55 | 1.52–13.6 | 0.007 | 2.68 | 1.01–7.11 | 0.047 |
| T stage (T1–3 vs T4) | 100.0 vs 80.0 | 3.75 | 1.19–11.8 | 0.025 | 2.42 | 1.00–5.86 | 0.048 |
| N stage (N0–2 vs N3) | 100.0 vs 88.5 | 2.34 | 1.01–5.40 | 0.048 | 1.91 | 1.00–4.20 | 0.049 |
| Histology (WHO type III vs II) | 87.5 vs 80.0 | 2.25 | 1.02–5.00 | 0.045 | 2.30 | 1.00–5.40 | 0.049 |
| Cisplatin cycles (≥ 5 vs < 5) | 91.7 vs 71.4 | 4.67 | 1.39–15.7 | 0.013 | 3.10 | 1.08–8.97 | 0.036 |
| Treatment delay >7 days (No vs Yes) | 90.3 vs 63.6 | 3.26 | 1.01–10.5 | 0.048 | 2.45 | 1.01–5.90 | 0.046 |

### 3.4. Treatment toxicity

**Table 4. Hematologic toxicities.**

| Toxicity | Grade 0 | Grade 1 | Grade 2 | Grade 3 |
|---|---|---|---|---|
| Leukopenia | 60.3% | 11.5% | 12.5% | 15.7% |
| Anemia | 82.8% | 2.2% | 10.8% | 4.3% |
| Thrombocytopenia | 100% | 0% | 0% | 0% |

Hematologic toxicities were generally mild. Table 4 shows that no patient developed thrombocytopenia, and no grade 4 hematologic toxicity occurred.

**Table 5. Non-hematologic toxicities.**

| Toxicity | Grade 1 | Grade 2 | Grade 3 |
|---|---|---|---|
| Skin (dermatitis) | 19.4% | 65.6% | 15.1% |
| Mucosa (mucositis) | 10.8% | 59.1% | 30.1% |
| Salivary (xerostomia) | 38.7% | 52.7% | 8.6% |

Non-hematologic toxicities are summarized in Table 5. No grade 4 skin, mucosal, or salivary gland (xerostomia) toxicity was observed. Notably, 15.1% of patients experienced grade 3 dermatitis, 30.1% had grade 3 mucositis, and 8.6% had grade 3 xerostomia. No cases of renal toxicity were recorded.

## 4. DISCUSSION

### 4.1. Response to treatment

At 3 and 6 months after treatment, the overall complete response rates in our study were 89.2% and 87.1%, respectively. The primary tumor CR was 92.4%, and the nodal CR was 96.7% at 3 months and 95.6% at 6 months.

Our outcomes are higher than those reported by Đặng Huy Quốc Thịnh [3] (n = 121), who found overall, primary, and nodal complete response rates of 75.2%, 85.1%, and 75.2%, respectively. This difference may be attributable to radiotherapy techniques: Thịnh's study used 2D and 3D conformal radiotherapy, whereas our patients were treated with IMRT. This is consistent with international studies demonstrating the advantages of IMRT over 2D and 3D-CRT in NPC radiotherapy [1,2].

Compared with other studies, Hoàng Đào Chinh [4] (n = 57) reported an overall complete response rate of 96.5%. In the study by Chen et al. [5] (n = 249), patients with stage III–IVB NPC received concurrent chemoradiotherapy

with low-dose cisplatin followed by three cycles of adjuvant PF chemotherapy; 43% of patients received IMRT. The complete response rate in the Chen et al. trial was 99.6%. These findings underscore the high chemosensitivity of NPC and the effectiveness of concurrent chemoradiotherapy in achieving locoregional control for advanced-stage disease.

All three patients with persistent nodal disease after CCRT had a history of cervical lymph node biopsy, and the nodes subsequently progressed with invasion into the deep fascia, adjacent muscles, and overlying skin. Clinically, this appears to be a poor prognostic feature, and the literature has reported reduced responses to CCRT in similar settings.

For example, a 59-year-old woman (C.T.D.) with stage IVA NPC (T1N3M0) was diagnosed by cervical nodal biopsy. The node enlarged and invaded surrounding tissues after surgery. She received definitive CCRT (70 Gy) and completed six weekly cisplatin cycles; at 6 months, recurrence occurred in the right preauricular/postauricular nodes, which is atypical for NPC and may reflect iatrogenic dissemination from incomplete nodal excision. Despite salvage neck dissection and adjuvant chemotherapy after tumor board review, bilateral cervical nodal progression developed two months later. In patients with malignant cervical nodes and no clear primary on CT/MRI, excisional biopsy may be necessary when PET/CT is unavailable; however, incomplete excision may increase the risk of tumor seeding, underscoring the importance of multidisciplinary management.

### 4.2. Factors influencing treatment response

Patients with stage II–III disease were significantly more likely to achieve complete response than those with stage IVA. This finding aligns with expected tumor burden and biology: T4 primary tumors and extensive N3 nodal disease may be more hypoxic and may invade critical structures (e.g., brainstem, cranial nerves, salivary glands), which limits the radiation dose that can be safely delivered.

These findings are consistent with the study by Phạm Sơn Lâm [6], which reported a complete response (CR) rate at the primary tumor of 96.2% in the T1–T3 group, compared with 76.9% in T4 disease; patients with N3 nodal status had a nodal CR rate nearly 30% lower than those with N1–N2. According to Hoàng Đào Chinh [4], patients with T4 tumors, a large total nodal volume (>60 $cm^3$), or deep cervical lymph node involvement (levels IIb–V) had markedly lower complete response rates, despite receiving the same concurrent chemoradiotherapy regimen. The ASCO guidelines also emphasize that T4 disease carries a high risk of locoregional treatment failure, which

consequently affects response at both the primary tumor and nodal sites.

### 4.3. Toxicity of the regimen

Hematologic toxicity: grade 3 leukopenia and anemia occurred in 15.7% and 4.3% of patients, respectively, with no grade 4 hematologic toxicity and no thrombocytopenia. These findings are comparable to other domestic studies. For example, Nguyễn Anh Tuấn [7] reported that 11.3% of patients experienced grade ≥3 leukopenia, and Trần Thị Kim Phượng [8] reported a 9.7% rate of grade 3 leukopenia with no grade 3 anemia.

Non-hematologic toxicity: grade 3 dermatitis, mucositis, and xerostomia were observed in 15.1%, 30.1%, and 8.6% of patients, respectively, with no grade 4 events. These toxicity rates are similar to those reported by Hoàng Đào Chinh [4] and Võ Văn Xuân [9], and lower than those reported by Đặng Huy Quốc Thịnh [3]. This difference may be attributable to the radiotherapy technique used (IMRT versus 3D-CRT).

## 5. CONCLUSION

Concurrent chemoradiotherapy using IMRT combined with weekly low-dose cisplatin for stage II–IVA nasopharyngeal carcinoma is an effective standard treatment, achieving a high complete response rate with acceptable toxicity. Patients with stage IVA disease, T4 primary tumors, or N3 nodal status had lower complete response rates compared with other stages. In contrast, WHO type III histology, completion of the planned chemotherapy course, and absence of prolonged treatment delays were associated with higher complete response rates.

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