TPM Vol. 32, No. S9, 2025
ISSN: 1972-6325
https://www.tpmap.org/

Open Access

EVALUATING THE CLINICAL OUTCOME IN HYPOPHARYNGEAL SQUAMOUS CELL CARCINOMA PATIENTS TREATED WITH CARBOPLATIN/PACLITAXEL BASED INDUCTION CHEMOTHERAPY FOLLOWED BY CONCURRENT CHEMORADIATION

DR. JAWAD LATIF
RESIDENT CLINICAL AND RADIATION ONCOLOGY DEPARTMENT, SHAUKAT KHANUM MEMORIAL CANCER HOSPITAL AND RESEARCH CENTRE, dr.jawadlatif1@gmail.com

DR. IRFAN HAIDER
CONSULTANT AND HEAD OF DEPARTMENT CLINICAL AND RADIATION ONCOLOGY SHAUKAT KHANUM MEMORIAL CANCER HOSPITAL AND RESEARCH CENTRE PESHAWAR.

DR. MUHAMMAD FAWAD UL QAMAR
CONSULTANT CLINICAL AND RADIATION ONCOLOGY, SHAUKAT KHANUM MEMORIAL CANCER HOSPITAL AND RESEARCH CENTRE PESHAWAR

DR. YASIR INAM
SENIOR INSTRUCTOR CLINICAL AND RADIATION ONCOLOGY, SHAUKAT KHANUM MEMORIAL CANCER HOSPITAL AND RESEARCH CENTRE

DR. DANYAL SAMI
RESIDENT CLINICAL AND RADIATION ONCOLOGY, SHAUKAT KHANUM MEMORIAL CANCER HOSPITAL AND RESEARCH CENTRE.

DR. MOHAMMAD UZAIR
RESIDENT CLINICAL AND RADIATION ONCOLOGY, SHAUKAT KHANUM MEMORIAL CANCER HOSPITAL AND RESEARCH CENTRE.

Published :- 15 December 2025

ABSTRACT

Background: Cisplatin-based chemotherapy, used either as induction therapy or concurrently with radiotherapy, remains a standard treatment option for head and neck squamous cell carcinoma.

Objective: To evaluate tumor response, treatment tolerance, disease-free survival, and progression-free survival in patients with non-metastatic hypopharyngeal squamous cell carcinoma treated with carboplatin-paclitaxel-based induction chemotherapy followed by concurrent chemoradiation.

Methodology: This single-arm prospective study included 57 patients with non-metastatic hypopharyngeal squamous cell carcinoma and conducted in Clinical and Radiation Oncology Department, Shaukat Khanum Memorial Cancer Hospital and Research Centre Peshawar from June 2025 to November 2025. Patients received carboplatin-paclitaxel-based induction chemotherapy followed by weekly concurrent chemoradiation using the same chemotherapy regimen. Treatment tolerance, compliance, and toxicity were recorded at regular intervals. Acute toxicities were assessed within 90 days from treatment initiation, while late toxicities were evaluated 6 months after completion of chemoradiation using RTOG and CTCAE grading criteria.

Results: All 57 evaluable patients received the planned treatment. Complete clinical and radiological response was observed in 29 patients (50.87%), while partial response was noted in 8 patients (14.03%). Stable disease was observed in 12 patients (21.05%), and progressive disease occurred in 8 patients (14.03%). At last follow-up, 35 patients were alive (61.4%; 95% CI: 48.4–72.9), 12 patients had died (21.05%; 95% CI: 12.5–33.3), and 10 patients were lost to follow-up (17.54%; 95% CI: 9.8–29.4). Progression-free survival at 3 and 6 months was 85.3% and 80.0%, respectively, while disease-free survival was 87.4% and 82.2%,

respectively. Acute skin toxicity occurred in 36 patients (63.16%), acute dysphagia in 38 (66.66%), mucositis in 44 (77.19%), and xerostomia as late toxicity in 25 (43.85%).
Conclusion: Carboplatin-paclitaxel-based induction chemotherapy followed by concurrent chemoradiation appeared to be a tolerable and effective treatment approach for non-metastatic hypopharyngeal squamous cell carcinoma.
KEYWORDS: Chemoradiation, head and neck cancer, hypopharyngeal squamous cell carcinoma, induction chemotherapy, carboplatin, paclitaxel.

INTRODUCTION

Treating Hypopharyngeal Squamous Cell Carcinomas with laryngeal preservation has been proven possible as per European organization for the research and treatment of cancer in their Phase III Trial (EORTC 24954) without compromising overall survival; however, the results were still not striking in terms of disease control, recurrence rates and overall survival, which is reported to be only 30% [1]. Their induction chemotherapy was cisplatin and 5-fluorouracil based. We treated our patients with Carboplatin/ Paclitaxel based induction and concurrent chemoradiotherapy with conventional Fractionation, while keeping in view of poor outcome of the EORTC Phase III Trial and poor tolerance of cisplatin-based chemotherapy in our population. Hypopharyngeal cancer is a rare disease with annual incidence of 0.5% of all human cancers and 3-5% of all head and neck cancers [2,3]. Squamous cell carcinoma is the most common histology, accounting for more than 95% of cases, and often diagnosed at an advanced stage [4]. Thus, it is associated with unfavorable prognosis, submucosal spread, regional nodal involvement and increased rate of distant metastasis. Approximately, 50% of the patients develop recurrence in less than 1 year [5]. Overall 5 years survival is 22-30% in locally advanced Hypopharyngeal cancers since the past few decades [6,7]. It remains controversial whether which treatment strategy is optimal for treating Hypopharyngeal cancers. Historically, all the resectable Hypo pharyngeal cancers were treated with surgery with the expense of laryngectomy followed by adjuvant radiotherapy that had greatly impaired the quality of life [8]. However, many prospective studies have evaluated that organ preservation without compromising on overall survival is possible with implementation of induction chemotherapy followed by radiation [9,10]. European Organization for Research and Treatment of cancer in their Phase III trial (EORTC 24891) concluded safe preservation of larynx with induction chemotherapy and radiation in Hypopharyngeal cancer patients [11]. The 10 years results of this trial were conclusive as that showed no change in PFS and OS allowing more than half of the survivors to retain their larynx [12]. The treatment modality conversion from surgery followed by adjuvant radiation to induction chemotherapy followed by radiation or concurrent chemoradiation has no impact on outcome in terms of overall survival or disease-free survival rates. However, the striking change that these prospective studies showed is that survived patients can retain their larynx [13].

Objectives

- To investigate tumor response to the treatment that we offer.
- To determine clinical and radiological response soon after completion of treatment.
- To evaluate disease free survival and progression free survival.
- To assess the response rates, toxicity profiles and recurrence patterns.
- To prove the efficacy of induction chemotherapy.

METHODOLOGY

This was a single-arm prospective study conducted in Clinical and Radiation Oncology Department, Shaukat Khanum Memorial Cancer Hospital and Research Centre Peshawar from June 2025 to November 2025. A total of 57 patients with histologically confirmed non-metastatic hypopharyngeal squamous cell carcinoma were enrolled in the study. Non-probability consecutive sampling technique was used. Patients aged 18 to 70 years with histologically confirmed non-metastatic hypopharyngeal squamous cell carcinoma, ECOG performance status 0–2, no contraindication to chemotherapy, and willingness to provide written informed consent were included. Patients with metastatic disease at presentation, prior radiotherapy for head and neck malignancy, previous chemotherapy for current disease, histological types other than squamous cell carcinoma, poor performance status, inability to complete induction chemotherapy, refusal to participate, or withdrawal of consent during treatment were excluded.

Data Collection

After obtaining approval from the institutional ethical review committee and written informed consent from all participants, eligible patients were enrolled following a comprehensive clinical assessment. Baseline demographic and clinical information, including age, gender, tumor site, tumor stage, histopathological grade, hematological and biochemical investigations, performance status, and baseline radiological imaging findings, were recorded on a structured proforma.

All enrolled patients received induction chemotherapy consisting of carboplatin at AUC 5 and paclitaxel at a dose of 175 mg/m² administered every three weeks for three cycles. Following induction chemotherapy, patients were clinically reassessed for treatment tolerance, toxicity, and response before proceeding to concurrent

chemoradiotherapy. Radiotherapy planning was performed using simulation CT, and treatment was delivered using VMAT/Rapid Arc technique with megavoltage photon beams. Radiation doses included 70 Gy in 35 fractions to the high-risk disease volume, 63 Gy in 35 fractions to the intermediate-risk volume, and 56 Gy in 35 fractions to low-risk nodal regions. Concurrent chemotherapy consisted of weekly carboplatin at AUC 2 and paclitaxel at 50 mg/m² for five cycles administered during radiotherapy. Patients were assessed regularly for toxicity monitoring, initially after completion of induction chemotherapy and then weekly during concurrent chemoradiotherapy. Acute toxicities occurring within 90 days of treatment initiation and late toxicities assessed at 3 and 6 months after treatment completion were documented according to RTOG and CTCAE grading criteria. Tumor response was evaluated through clinical examination and radiological imaging using CT or MRI according to RECIST criteria and categorized as complete response, partial response, stable disease, or progressive disease. Disease-free survival and progression-free survival were also assessed during follow-up. Primary outcome measures included tumor response, treatment tolerance, treatment compliance, acute toxicity profile, and late toxicity profile. Secondary outcomes included disease-free survival and progression-free survival.

Statistical Analysis

Data were analyzed using SPSS version 26.0. Continuous variables were expressed as mean ± standard deviation, while categorical variables were presented as frequencies and percentages. Tumor response categories were analyzed according to RECIST criteria. Toxicity variables were graded according to RTOG and CTCAE systems and analyzed using chi-square test where appropriate. Disease-free survival and progression-free survival were calculated using survival analysis methods. A p-value of ≤0.05 was considered statistically significant.

RESULTS

A total of 57 patients with non-metastatic hypopharyngeal squamous cell carcinoma were included in the study. A total of 57 patients were included, with a slight male predominance, 32 (56.14%), compared with 25 (43.85%) females. The post-cricoid region was the most common tumor subsite, seen in 46 (80.70%) patients, followed by posterior pharyngeal wall in 6 (10.52%) and pyriform sinus in 5 (8.78%). Most patients presented with advanced disease, with stage III in 30 (52.63%) and stage IVA in 23 (40.35%). Grade II tumors were most frequent, observed in 45 (78.94%) patients. All patients received carboplatin-paclitaxel-based treatment. Induction chemotherapy consisted of carboplatin AUC 5 plus paclitaxel 175 mg/m² every 3 weeks for 2 cycles, followed by concurrent chemoradiotherapy using carboplatin AUC 2 plus paclitaxel 50 mg/m² weekly for 5 cycles. Radiation therapy was delivered according to risk volume, with 70 Gy/35 fractions to high-risk volume, 63 Gy/35 fractions to intermediate-risk volume, and 56 Gy/35 fractions to low-risk volume.

Table 1. Baseline and tumor characteristics of study patients (n = 57)

Variable	n (%)
Male	32 (56.14)
Female	25 (43.85)
Post-cricoid subsite	46 (80.70)
Posterior pharyngeal wall	6 (10.52)
Pyriform sinus	5 (8.78)
Stage II	4 (7.01)
Stage III	30 (52.63)
Stage IVA	23 (40.35)
Grade I	6 (10.52)
Grade II	45 (78.94)
Grade III	6 (10.52)

According to RECIST version 1.1, complete response was achieved in 29 (50.87%) patients, while partial response was noted in 8 (14.03%). Stable disease was observed in 12 (21.05%) patients, and progressive disease occurred in 8 (14.03%). Overall, more than half of the patients achieved complete clinical and radiological response. Grade ≥2 treatment-related toxicities were commonly observed. Mucositis was the most frequent toxicity, affecting 44 (77.19%) patients, followed by dysphagia in 38 (66.66%) and skin toxicity in 36 (63.16%). Xerostomia was reported as a late toxicity in 25 (43.85%) patients.

Table 2. Treatment Response According to RECIST 1.1 and Treatment-Related Toxicities of Grade ≥2

Domain	Variable / Category	n (%)
Treatment response according to RECIST 1.1	Complete response	29 (50.87%)
	Partial response	8 (14.03%)
	Stable disease	12 (21.05%)
	Progressive disease	8 (14.03%)
Treatment-related toxicities of grade ≥2	Skin toxicity	36 (63.16%)
	Mucositis	44 (77.19%)

	Dysphagia	38 (66.66%)
	Xerostomia as late toxicity	25 (43.85%)

The 3-month and 6-month progression-free survival rates were 85.3% and 80.0%, respectively. Disease-free survival was 87.4% in 3 months and 82.2% at 6 months, showing maintained short-term disease control after treatment.

Table 3. Survival outcomes after treatment

Endpoint	Median, months	3 months	6 months
Progression-free survival	Not reached	85.3%	80.0%
Disease-free survival	Not reached	87.4%	82.2%

DISCUSSION

The Management of Non-Metastatic Hypopharyngeal squamous cell carcinoma remains a clinical challenge due to aggressive nature of the disease and the high prevalence of advanced stages presentation of these patients. Historically, the standard of care involved surgery followed by adjuvant radiotherapy, which often necessitated a total laryngectomy ultimately impairing the quality of life. Our study demonstrates that a Carboplatin-Paclitaxel based induction and concurrent chemoradiotherapy regimen offers a highly effective and tolerable alternative for organ preservation. The clinical outcomes in this cohort are particularly significant when compared to historical benchmark studies. While literature suggests that roughly 50% of hypopharyngeal cancer patients develop recurrence less than one year, our study achieved a 6-months progression free survival (PFS of 85.3 months). Furthermore, our survival rates compared favorably to the EORTC 24954 Phase III trial, which utilized a cisplatin and 5-fluorouracil-based induction and reported an overall survival of only 30%. In contrast, 61.4% of our patients were alive at the last follow-up, supporting the conclusion that this regimen provides excellent tumor control, therefore induction chemotherapy must be considered in eligible patients [14]. A primary motivation for this study was the poor tolerance of cisplatin-based chemotherapy in our patient population, which often leads to treatment interruptions and compromised disease control. Our findings confirm that the Carboplatin-Paclitaxel alternative is manageable [15]. Although acute mucositis was prevalent (77.19%), it is critical to note that only 10.52% of patients experienced Grade 3 severity, and late toxicities like xerostomia remained within acceptable limits (43.85%). This improved toxicity profile facilitates higher compliance, which is essential for successful concurrent chemoradiation. Beyond survival, the success of larynx preservation is a key finding. By achieving a Complete Response (CR) in 50.87% of patients, this non-surgical approach aligns with the goals of the EORTC 24891 trial, which proved that induction chemotherapy allows survivors to retain their larynx without compromising overall survival [16]. Our results suggest that this regimen provides a viable path for patients to avoid the functional morbidity associated with a laryngectomy while maintaining high rates of disease-free survival. Despite these positive outcomes, this study has limitations. The loss to follow-up rate of 17.5% (10 patients) represents a challenge for long-term survival analysis and reflects the socio-demographic difficulties in maintaining continuous monitoring in our population. Additionally, as a single-arm prospective study, these results would benefit from further validation through multi-center randomized controlled trials to compare this regimen directly against modern cisplatin-based protocols [17].

This study had some limitations. First, it was a single-arm study without a control or comparison group, so direct comparison with cisplatin-based chemoradiation could not be performed. Second, the sample size was relatively small, with only 57 patients, which may limit the generalizability of the findings. Third, follow-up duration was short, with survival outcomes assessed only up to 6 months, so long-term disease control, recurrence, and late toxicity could not be fully evaluated. Fourth, some patients were lost to follow-up, which may have affected survival estimates. Lastly, treatment response was assessed clinically and radiologically, but longer follow-up and larger comparative trials are needed to confirm the efficacy and safety of carboplatin-paclitaxel-based chemoradiation in this patient population.

CONCLUSION

Induction chemotherapy should be considered for eligible patients. The Carboplatin-Paclitaxel based regimen is a well-tolerated and effective treatment approach, offering improved disease control. Its favorable safety profile and durability make it perfectly suitable for concurrent use with radiation therapy, especially when compared with historical outcomes. Importantly it serves as a valuable alternative for patients who are not ideal candidates for standard cisplatin-based regimens.

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