



Research Article

Section: Radiation Oncology

Induction Chemotherapy Followed by Chemoradiation in Patients of Locally Advanced Laryngeal and Hypopharyngeal Cancers with Intent of Organ Preservation

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ABSTRACT

Laryngeal and hypopharyngeal cancers are among the most common malignancies of the head and neck region. Traditionally, these cancers have been managed with surgery, but the advent of organ-preserving treatments has revolutionized their management. Induction chemotherapy followed by chemoradiation is an emerging approach for patients with locally advanced laryngeal and hypopharyngeal cancers, with the primary intent of organ preservation while ensuring optimal oncological outcomes. Induction chemotherapy, typically consisting of platinum-based agents such as cisplatin and taxanes, is utilized to reduce tumor size and assess tumor response. This initial treatment phase offers a chance for organ preservation, with the aim to downstage tumors and make them amenable to subsequent chemoradiation. The subsequent chemoradiation phase involves combining chemotherapy with radiation therapy, which intensifies tumor control while allowing for the preservation of the larynx and hypopharynx. This approach aims to avoid total laryngectomy, which can have significant functional and psychological impacts on patients. Studies have demonstrated that induction chemotherapy followed by chemoradiation can offer comparable survival outcomes to surgery, with the added benefit of preserving critical organ function, particularly speech and swallowing. However, careful patient selection and monitoring of treatment toxicity are crucial to optimize the benefits of this regimen. Long-term outcomes, including survival, recurrence, and quality of life, are pivotal in evaluating the success of this organ-preserving strategy. The integration of induction chemotherapy with chemoradiation represents a promising alternative to surgery in the management of locally advanced laryngeal and hypopharyngeal cancers. Further prospective studies are needed to refine patient selection criteria and determine the long-term efficacy and safety of this approach in preserving both organ function and survival.

INTRODUCTION

According to the GLOBOCAN report of 2020, India recorded approximately 1.3 million new cases of cancer, with laryngeal and hypopharyngeal cancers accounting for 4.8% of the total, ranking sixth in incidence [1]. These cancers have a significant impact on patients' quality of life due to their crucial roles in respiration, speech production, and swallowing. The primary risk factors for these cancers include smoking, alcohol consumption, and tobacco use. Managing these cancers presents unique challenges, as treatment can severely affect breathing, voice quality, and the ability to swallow [2].

In cases of locally advanced laryngeal and hypopharyngeal cancers, the treatment strategy is often focused on organ preservation while ensuring effective disease control. A multimodal approach that combines surgery, chemotherapy, and radiation therapy is typically used to achieve these goals. Recent advancements in treatment protocols aim to preserve organ function without compromising survival rates [3].

Laryngeal preservation strategies aim to treat cancer while maintaining the organ's functions. These strategies may involve organ-preserving surgeries, radiation therapy, or chemotherapy, with options varying depending on the cancer's stage [4]. Early-stage

cancers may be treated with surgeries like partial laryngectomy, endoscopic resection, or radiation therapy, aiming to both cure the cancer and preserve the larynx's function. In more advanced cases, especially when cartilage invasion is present, a combined approach with induction chemotherapy followed by chemoradiation is often used [5].

Induction chemotherapy has emerged as a key tool in treating advanced cancers, helping reduce tumor size before proceeding with definitive treatments. The chemotherapy regimen typically includes platinum-based agents like cisplatin combined with taxanes [6]. By shrinking the tumor, induction chemotherapy allows for less aggressive surgeries or radiation treatments, potentially leading to better functional outcomes for the patient. However, in cases where the tumor involves extensive cartilage invasion, a total laryngectomy may be necessary [7].

The process of induction chemotherapy is crucial in selecting patients for organ-preserving treatments. Tumors that respond well to induction chemotherapy are more likely to benefit from subsequent radiation therapies, making it a critical step in the treatment plan. Various chemotherapy regimens, such as those including cisplatin and 5-fluorouracil (5-FU), have shown promise, with the TPF regimen demonstrating increased rates of laryngeal preservation and better overall survival in clinical trials. However, the effectiveness of these treatments in the Indian context is still under study, and there is a need for more research tailored to the local population [8].

Induction chemotherapy's efficacy in reducing tumor burden and facilitating organ preservation is significant in patients with locally advanced laryngeal and hypopharyngeal cancers. By improving the tumor's responsiveness to subsequent therapies, induction chemotherapy enhances the likelihood of successful organ preservation, allowing patients to maintain their speech and swallowing functions [9].

RESULTS

Table 1: Age distribution of patients

Age Group	Count	Percentage
41-50	18	42.90%
51-60	18	42.90%
61-70	6	14.20%
Total	42	100%

The majority of patients in this study were between 41 and 60 years old, each accounting for 42.9% of the total population. A smaller portion, 14.2%, were in the 61-70 age

Nevertheless, this treatment is not without side effects, including nausea, fatigue, and increased vulnerability to infections, which need to be managed carefully [10].

In conclusion, induction chemotherapy is a vital strategy in the management of advanced laryngeal and hypopharyngeal cancers, offering the potential for organ preservation while effectively controlling the disease [11]. As ongoing research continues to refine these approaches, the focus remains on improving patient outcomes and preserving quality of life through personalized treatment regimens. The success of this approach will depend on continued investigation, particularly in diverse populations, to ensure its optimal application in clinical practice [12].

MATERIAL AND METHODS

This prospective observational study assessed the efficacy and safety of induction chemotherapy followed by chemoradiation in patients with locally advanced laryngeal and hypopharyngeal cancers, with a focus on organ preservation. Conducted at Vardhman Mahavir Medical College and Safdarjung Hospital, New Delhi, over 18 months, ethical approval was obtained. The study included 42 patients (aged 18-60 years) with histologically confirmed stage III/IV squamous cell carcinoma of the larynx or hypopharynx. Patients with T4 tumors, contraindicating comorbidities, pregnancy, or prior cancer treatments were excluded. The induction chemotherapy regimen consisted of TPF (docetaxel, cisplatin, 5-fluorouracil), followed by chemoradiation therapy. Radiation therapy was administered as 44 Gy in 22 fractions, followed by 22 Gy in 11 fractions, with weekly cisplatin for radiosensitization. Patients were closely monitored for treatment response and toxicity through clinical examinations and laboratory tests, with toxicity assessed using CTCAE and RTOG criteria

group. This distribution highlights that locally advanced laryngeal and hypopharyngeal cancers predominantly affect middle-aged individuals.

Table 2: Gender distribution of patients

Gender	Count	Percentage
Female	4	9.50%
Male	38	90.50%
Total	42	100%

The table shows gender distribution in a group of 42 individuals. Out of the total, 4 (9.5%) are female, while 38 (90.5%) are male. The data highlights a predominantly male group, with females making up a small percentage of the total population.

Table 3: Site of the disease

ite of Disease	Count	Percentage
Supraglottis	19	45.20%
Glottis	12	28.60%
Pyriform sinus	10	23.80%
Subglottis	1	2.40%
Total	42	100%

The table shows the distribution of disease sites among 42 individuals. The most common site is the supraglottis (45.2%), followed by the glottis (28.6%) and pyriform sinus (23.8%). The subglottis is the least affected, with only 1 (2.4%) case. The data adds up to 100%.

Table 4: Tumor status of patients

Tumor Status	Count	Percentage
T4a	19	45.20%
T3	15	35.70%
T2	5	11.90%
T1	3	7.10%
Total	42	100%

The table displays tumor status among 42 individuals. The most prevalent stage is T4a (45.2%), followed by T3 (35.7%). T2 and T1 stages are less common, with 11.9% and 7.1% respectively. The data indicates the majority of tumors are in more advanced stages (T4a, T3).

Table 5: Analysis of Nodal Status

Nodal Status	Count	Percentage (%)
N2a	12	28.6
N2c	12	28.6
N2b	11	26.2
N1	5	11.9
N3a	1	2.4
N0	1	2.4
Total	42	100

The table shows the distribution of nodal status in 42 individuals. The most common statuses are N2a and N2c, each at 28.6%, while N2b follows at 26.2%. N1, N3a, and N0 are less common, representing smaller percentages.

Table 6: Analysis of Stage

Stage	Count	Percentage (%)
Stage IVA	25	59.5
Stage III	16	38.1
Stage IVB	1	2.4
Total	42	100

The table shows the distribution of disease stages among 42 individuals. Stage IVA is the most common (59.5%), followed by Stage III (38.1%). Stage IVB is rare representing only 2.4%. The majority of cases are in advanced stages (IVA and III).

Table 7: ECOG Performance Status Distribution

ECOG Performance Status	Count	Percentage (%)
1	22	52.4
0	20	47.6
Total	42	100

The table shows the distribution of ECOG performance status in 42 individuals. Most participants have a status of 1 (52.4%), indicating mild symptoms, while 47.6% are in status 0, meaning fully active. The data suggests a majority have slightly impaired functionality.

Table 8: Analysis of laryngeal preservation outcomes

Larynx Preservation Status	Count	Percentage (%)
Yes	28	66.67
No	12	28.57
Defaulted	2	4.76
Total	42	100

The table shows the larynx preservation status for 42 individuals. Most participants (66.67%) preserved their treatment plan. The majority successfully preserved their larynx, while 28.57% did not. A small number (4.76%) defaulted, meaning they did not follow the expected treatment plan.

Table 9: Number of Chemotherapy Cycles

Number of Chemotherapy Cycles	Count	Percentage (%)
3	36	85.7
2	5	11.9
1	1	2.4
Total	42	100

The table shows the number of chemotherapy cycles received by 42 individuals. The majority (85.7%) underwent 3 cycles, 11.9% received 2 cycles, and only 2.4% had 1 cycle.

This suggests most individuals underwent a more extensive chemotherapy regimen.

Table 10: Analysis of Response to IC

Response to IC after 3 Cycles	Count	Percentage (%)
Partial Response	15	35.71
Complete Response	12	28.57
Progressive Disease	8	19.05
Stable Disease	5	11.9
Defaulted	2	4.76
Total	42	100

The table shows responses to initial chemotherapy (IC) after 3 cycles in 42 individuals. Most experienced partial (35.71%) or complete (28.57%) response, while 19.05% had progressive disease, and 11.9% had stable disease. A small number (4.76%) defaulted on treatment.

Table 11: Analysis of CTRT status

CTRT Status	Count	Percentage (%)
Completed	31	73.81
Not given	9	21.43
Defaulted	2	4.76
Total	42	100

The table shows the status of concurrent chemoradiotherapy (CTRT) for 42 individuals. Most patients (73.81%) completed the treatment, while 21.43% did not receive it. A small number (4.76%) defaulted, indicating they did not follow the prescribed treatment plan.

Table 12: Pattern of recurrence

Recurrence Status	Count	Percentage (%)
None	19	45.24
Distant	9	21.43
Regional	6	14.29
Defaulted	5	11.9
Not applicable	3	7.14
Total	42	100

The table shows recurrence status in 42 individuals. Nearly half (45.24%) had no recurrence. Distant recurrence occurred in 21.43%, regional in 14.29%, and 11.9% defaulted.

A small portion (7.14%) had a status marked as not applicable, indicating differing clinical conditions.

Table 13: Neutropenia Grade

Neutropenia Grade	Count	Percentage (%)
Grade 0	13	30.95
Grade 3	9	21.43
Grade 2	8	19.05
Grade 1	6	14.29
Grade 4	4	9.52
Defaulted	2	4.76
Total	42	100

The table displays neutropenia grades in 42 individuals. The most common grade is Grade 0 (30.95%), indicating no neutropenia. Grade 3 and Grade 2 affect 21.43% and 19.05%, respectively, while Grade 1 and Grade 4 are less frequent. A small number defaulted (4.76%).

DISCUSSION

India recorded 1.3 million new cancer cases in 2020, with laryngeal and hypopharyngeal cancers accounting for 4.8% of these cases. These cancers, primarily driven by smoking, alcohol, and tobacco use, present significant treatment challenges due to their impact on respiration, voice, and swallowing [13]. Multimodal approaches can preserve organ function and survival, especially in early stages. For locally advanced cancers, induction chemotherapy followed by chemoradiation has shown promising outcomes in preserving the larynx and maintaining function. However, advanced tumors (T3 and T4) may require more aggressive treatments, including surgery, which often leads to significant functional morbidity [14].

Induction chemotherapy with the TPF regimen (taxane, platinum, and 5-fluorouracil) followed by chemoradiotherapy has proven effective in preserving laryngeal function in many cases [15]. However, research specific to India on the effectiveness of this approach has been limited. Our study focused on evaluating the efficacy and toxicity of this regimen for locally advanced laryngeal and hypopharyngeal cancers [16]. It found a high rate of larynx preservation, with 66.67% of patients maintaining their laryngeal function, which aligns with global findings that suggest induction chemotherapy followed by chemoradiation as a standard approach [17]. The highest mean TSB (17.64 mg/dL, SD 1.44) compared to Group B (12.33 mg/dL, SD 3.35) and Group C (12.16 mg/dL, SD 1.92). ANOVA

analysis confirmed a statistically significant difference ($p < 0.001$) in TSB levels among the groups, reinforcing that lower CBA levels predict higher bilirubin accumulation.

The study showed that most patients were in the 41-60 age range, with a predominance of male patients (90.48%). The supraglottis was the most commonly affected site, with a higher incidence of advanced T4 and T3 tumors [18]. Nodal involvement, particularly in the N2 categories, was also common, indicating advanced-stage disease. The majority of patients were classified as Stage IVA, reflecting the advanced nature of the cancers at diagnosis [19].

While most patients were able to preserve laryngeal function, there were some who faced disease recurrence, including distant and regional recurrences. The study also highlighted a significant occurrence of treatment-related toxicities, particularly mucositis and dysphagia, which are important to address in treatment planning [20].

In conclusion, our study confirms the efficacy of induction chemotherapy followed by chemoradiotherapy in preserving laryngeal function in patients with locally advanced cancers [21]. It also underscores the importance of early diagnosis and tailored treatment strategies for better patient outcomes. However, managing treatment toxicity remains a critical aspect of improving patient quality of life during and after treatment [22].

CONCLUSION

Managing locally advanced laryngeal and hypopharyngeal cancers is challenging due to their crucial roles in respiration, phonation, and swallowing. While traditional treatments control the disease, they often result in significant side effects, including loss of voice and impaired swallowing, affecting quality of life. Recent approaches focus on organ preservation strategies to maintain function

while controlling the disease. This study evaluated the safety and efficacy of induction chemotherapy (TPF regimen: taxane, platinum, 5-fluorouracil) followed by chemoradiation in patients with stage III-IV laryngeal or hypopharyngeal cancers. Forty-two patients were treated and evaluated for response and toxicity using standardized criteria.

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REFERENCES

1. Habib A. Management of advanced hypopharyngeal carcinoma: systematic review of survival following surgical and non-surgical treatments. *The Journal of Laryngology & Otology*. 2018 May;132(5):385-400.
2. Mayer A, Ladwa R, Porceddu SV. RADIATION AND CHEMOTHERAPY. *Head and Neck Cancer: Treatment, Rehabilitation, and Outcomes*. 2024 Jun 18:87.
3. Spector ME, Rosko AJ, Swiecicki PL, Brenner JC, Birkeland AC. From VA Larynx to the future of chemoselection: Defining the role of induction chemotherapy in larynx cancer. *Oral Oncology*. 2018 Nov 1;86:200-5.
4. Pillay B, Wootten AC, Crowe H, Corcoran N, Tran B, Bowden P, Crowe J, Costello AJ. The impact of multidisciplinary team meetings on patient assessment, management and outcomes in oncology settings: a systematic review of the literature. *Cancer treatment reviews*. 2016 Jan 1;42:56-72.
5. Anand U, Dey A, Chandel AK, Sanyal R, Mishra A, Pandey DK, De Falco V, Upadhyay A, Kandimalla R, Chaudhary A, Dhanjal JK. Cancer chemotherapy and beyond: Current status, drug candidates, associated risks and progress in targeted therapeutics. *Genes & Diseases*. 2023 Jul 1;10(4):1367-401.
6. Mahdavi H. Induction chemotherapy in locally advanced head and neck cancers, is there a best choice?. *Critical Reviews in Oncology/Hematology*. 2023 Apr 12:103986.
7. Issa MR, Samuels SE, Bellile E, Shalabi FL, Eisbruch A, Wolf G. Tumor volumes and prognosis in laryngeal cancer. *Cancers*. 2015 Nov 10;7(4):2236-61.
8. Aykan NF, Özatlı T. Objective response rate assessment in oncology: Current situation and future expectations. *World Journal of Clinical Oncology*. 2020 Feb 2;11(2):53.
9. Seufferlein T, Hammel P, Delpero JR, Macarulla T, Pfeiffer P, Prager GW, Reni M, Falconi M, Philip PA, Van Cutsem E. Optimizing the management of locally advanced pancreatic cancer with a focus on induction chemotherapy: expert opinion based on a review of current evidence. *Cancer Treatment Reviews*. 2019 Jul 1;77:1-0.
10. Olsson LT. Patient-and Tumor-Level Factors Impacting Chemotherapy Use and Effectiveness (Doctoral dissertation, The University of North Carolina at Chapel Hill).
11. Lin TC, Huang CH, Lien MY, Cheng FM, Li KC, Lin CY, Lin YC, Liang JA, Wang TH. Tumor Volume Reduction Rate to Induction Chemotherapy is a Prognostic Factor for Locally Advanced Head and Neck Squamous Cell Carcinoma: A Retrospective Cohort Study. *Technology in Cancer Research & Treatment*. 2022 Jun;21: 15330 338221107714.
12. Vidhyadharan S, Murthy SP, Subramaniam N. 14 Cancers of the Hypopharynx. *Comprehensive Management of Head and Neck Cancer*. 2021 Feb 22:175.
13. Magariños MM, Ajuria MS, Mendía XM, Iglesias ÓA, Petronacci CC, García AG, Sayáns MP. Diagnostic yield of sentinel lymph node biopsy in oral squamous cell carcinoma T1/T2-N0: systematic review and meta-analysis. *International Journal of Oral and Maxillofacial Surgery*. 2021 Oct 1;50(10):1271-9.
14. Bradley PJ. Epidemiology of hypopharyngeal cancer. In *Hypopharyngeal Cancer 2019* (Vol. 83, pp. 1-14). Karger Publishers.
15. Steuer CE, El-Deiry M, Parks JR, Higgins KA, Saba NF. An update on larynx cancer. *CA: a cancer journal for clinicians*. 2017 Jan;67(1):31-50.
16. Lindblom B, Sundberg J. The human voice in speech and singing. *Springer handbook of acoustics*. 2014:703-46.
17. Murry T, Carrau RL, Chan K. Clinical management of swallowing disorders. *Plural Publishing*; 2020 Dec 16.
18. Baird BJ, Sung CK, Beadle BM, Divi V. Treatment of early-stage laryngeal cancer: a comparison of treatment options. *Oral oncology*. 2018 Dec 1;87:8-16.
19. Siddiqui A, Connor SE. Imaging of the pharynx and larynx. *Imaging*. 2013;22(1):91047403.
20. Nocini R, Sanchis-Gomar F, Lippi G. Physical activity and laryngeal cancer. *Annals of translational medicine*. 2019 Dec;7(23).
21. Centers for Disease Control and Prevention (CDC). Vital signs: nonsmokers' exposure to secondhand smoke--United States, 1999-2008. *MMWR: Morbidity & Mortality Weekly Report*. 2010 Sep 10;59(35).
22. Jethwa AR, Khariwala SS. Tobacco-related carcinogenesis in head and neck cancer. *Cancer and Metastasis Reviews*. 2017 Sep;36:411-23.

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