ORIGINAL ARTICLE

The Role of Bilateral Versus Ipsilateral Neck Dissection in Oropharyngeal and Oral Cancer with Contralateral cN0 Neck in cT3 and cT4 Disease

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ABSTRACT

Introduction: Head and neck cancer (HNC) is a significant global health issue, with Head and Neck Squamous Cell Carcinoma (HNSCC) ranking among the most prevalent cancers worldwide. In particular, India faces high incidence rates due to tobacco and areca nut usage. While HNSCC primarily affects the oral cavity carcinoma (OC), larynx, and oropharyngeal carcinoma (OPC) outcomes are linked to HPV status and T-, N-, and M-status. The necessity of elective neck dissection (END) for contralateral clinically node-negative (cN0) necks remains debated, with limited literature on its impact. **Methodology:** This retrospective study analyzed 300 OC/OPC patients with contralateral cN0 necks who underwent bilateral or ipsilateral neck dissection. Data on patient demographics, tumor characteristics, and treatment outcomes were collected over three years. Survival analysis employed Kaplan-Meier techniques and Cox regression. **Result:** In OC/OPC, midline-reaching/crossing tumors were more common with bilateral neck dissection, but contralateral neck node metastasis was rare. There was no significant difference in OS or RFS between ipsilateral and bilateral neck dissection groups. **Conclusion:** Contralateral neck dissection in OC/OPC patients with clinically node-negative necks did not enhance OS or RFS. The potential benefits of wait-and-scan strategies warrant further investigation through prospective trials.

KEY WORDS: Head and Neck cancer (HNC), Oropharyngeal squamous cell carcinoma (OPC), Elective neck dissection (END), Recurrence free survival (RFS).

Introduction

Head and neck cancer (HNC) persists as a substantial global public health concern, manifesting in over 450,000 new cases worldwide annually[1]. According to the most recent GLOBOCAN estimates from 2020, Head and Neck Squamous Cell Carcinoma (HNSCC) ranks as the seventh most prevalent cancer globally, with approximately 890,000 new cases constituting approximately 4.5% of all global cancer diagnoses, and resulting in 450,000 deaths each year, Representing around 4.6% of global cancer-related mortality[2]. India exhibits the highest incidence rate, where up to 80% of all HNSCC cases are attributed to tobacco use, either alone or in conjunction with the areca nut[3]. Predominantly, HNSCC originates in the oral cavity, larynx and oro-/hypopharynx, and[4]. In oropharyngeal carcinoma (OPC), alongside human papillomavirus (HPV) status, the patient's prognosis is intrinsically linked to the T-, N-, and M-status[4,5].

The crucial prognostic factor for oral and oropharyngeal squamous cell carcinoma (OC, OPC) is the existence of metastasis of cervical lymph node[6]. The likelihood of such metastasis depends on the tumor's size and location[7,8]. At present, the gold standard in the surgical treatment of lymph node-positive (N +) oral and oropharyngeal cancer includes selective neck dissection, modified radical neck dissection, or radical neck dissection.[9–11]

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The issue of neck dissection on the ipsilateral side in clinically node-negative (N0) patients has been under consideration for the last five decades. Surgical strategies for addressing the N0 neck include elective neck dissection or careful observation, with therapeutic neck dissection applied in case of nodal relapse. However, the administration of elective neck dissection (END) concurrent with primary tumor resection has demonstrated an association with heightened overall survival (OS) and recurrence-free survival (RFS)[8,12–14]. Consequently, END for the ipsilateral clinically node-negative (cN0) neck is considered a conventional practice for oral cancer (OC) and oropharyngeal cancer (OPC). Despite this, debates persist regarding the necessity of performing END for the contralateral cN0 neck. Limited literature addresses this concern in the context of OC and OPC, with inconclusive evidence pertaining to OS and RFS outcomes[15–17].

In instances of oral and oropharyngeal cancer, this retrospective study aimed to determine if END of the contralateral cN0 neck results in enhanced OS and/or RFS, and whether such effects are dependent upon tumour size and the laterality of the originating location.

Materials and Methodology

Over a three-year period (January 1, 2016, to December 31, 2018), a cohort of 200 consecutively selected patients diagnosed with oral cancer (OC) or oropharyngeal cancer (OPC) and subjected to surgical interventions involving both ipsilateral and bilateral neck dissection in OPC and OC underwent meticulous scrutiny. To rule out patients with obvious involvement of lymph nodes, neck nodes were assessed using cervical clinical examination, computed tomography (CT), and/or magnetic resonance imaging (MRI). Following main staging, patients with probable contralateral lymph node manifestation were rigorously excluded from the research. When there were no palpable neck nodes on clinical findings and no pathological findings on any imaging modalities, the patient was classified as having contra-lateral (cN0) neck status.

Inclusion criteria: Newly diagnose case of SCC in oral cavity and oropharynx with clinically cT3 and cT4 stage disease and having contra-lateral N0 neck node status.

Exclusion criteria: Newly diagnose case of SCC in oral cavity and oropharynx with clinically positive contra-lateral neck node (cN+), Patients who had recurrent illness, those who had distant metastases at the time of diagnosis, those not receiving therapy in accordance with study procedures and other histologic subtypes like adenocarcinoma, dysplasia, carcinoma in situ are excluded. In this investigation, patients with tumour stages T1 and T2 were excluded.

The current research included 200 people with contralateral N0-neck status in total. Survival results and clinical parameters were collected retrospectively. Variables including age, gender, TNM status, pathological grading, methods of treatment, occurrences of death and recurrence or loss to follow-up were all rigorously gathered. Every participant received predetermined treatment plans that followed global criteria. These plans included adjuvant radiation for every person with positive nodes and chemotherapeutic escalation for extracapsular expansion and/or inadequate R-status. Those with missing data, poor staging information, and those who refused or did not finish treatment and/or conservative therapies (chemotherapy and radiation) were among the exclusion criteria for the survival analysis.

For this investigation, the average follow-up period was five years. Those who had ipsilateral neck dissection and those who had bilateral neck dissection comprised the two separate groups from which the total research cohort was divided. Prior to and after the surgical procedure, lymph node involvement was carefully categorised in relation to the next steps in the procedure, which led to the identification of three categories: (i) no involvement, (ii) ipsilateral metastasis, and (iii) bilateral metastasis. Macroscopic protrusions of at least 10 mm towards the midline were used to identify tumours whose expansions reached the midline; tumours that crossed the midline showed contralateral extensions.

The statistical analysis of group differences was conducted using the unpaired Student's t test for continuous variables and the Chi-square test and Fisher exact test for categorical data. In order to evaluate the primary outcomes, overall survival (OS) and recurrence-free survival (RFS), the time interval between the start of therapy and any cause death or recurrence was measured. The assessment of the cancer risks associated with elective contralateral neck dissection was limited to patients in whom there was no reason to suspect involvement of the

contralateral lymph nodes.

In particular, a thorough analysis of overall survival and recurrence-free survival was carried out with regard to oral and oropharyngeal carcinomas. Recurrence-free survival was examined with a focus on lymph node recurrence in order to assess the direct effect of the wait-and-scan strategy in patients who had contralateral neck-negative status. Notably, the recurrence-free survival study did not include individuals who had distant metastases or recurrence at the initial tumour location.

The Kaplan-Meier technique was used to calculate the survival rates and associated curves, which were then further assessed using the log-rank test for univariate analysis. After being found to have prognostic or effect-modifying potential in univariate analysis, variables were evaluated in multivariate analysis using proportional Cox regression. P values less than 0.05 were considered statistically significant. GraphPad 4.0 made statistical analysis easier to carry out.

Result

Patient/Tumor characteristics and survival in oral cancer (OC) patients

In the current study, 200 patients with oral cancer (OC) were enrolled one after the other. Of these, one hundred patients had bilateral neck dissection while the other hundred patients had ipsilateral neck dissection. At the time of diagnosis, the patients were 50 years old on average, with a significant male preponderance; nevertheless, there were no appreciable variations in the groups' age and gender distribution (Table 1).

When OC patients had bilateral neck dissection, the frequency of midline-reaching/crossing tumours was substantially greater ($p < 0.0001$) than when patients had ipsilateral neck dissection (Table 1). Only 02 individuals were found to be positive for pathological contralateral neck node metastasis out of the 100 patients without B/L neck dissection in OC; the remaining 07 patients were diagnosed with pathological no neck nodes (pN0), 191 patients with pathological ipsilateral neck node metastasis.

Patients with lymph node positive, or elevated T-status ($\geq$ T3) were advised to have adjuvant radiation treatment. Furthermore, patients with nodal involvement (N+) exhibiting extracapsular extension or inadequate R-status received adjuvant radio chemotherapy.

When OC patients' overall survival (OS) and recurrence-free survival (RFS) were examined, patients who had ipsilateral neck dissection had an OS of 56 months on average, whereas patients who had bilateral neck dissection had an OS of 54 months ($p = 0.51$).

Patient/Tumor characteristics and survival in oropharyngeal cancer (OPC) patients

This study included 100 patients with oropharyngeal cancer, of whom 50 received ipsi-lateral neck dissection and the remaining 50 underwent bi-lateral neck dissection. Compared to patients treated with ipsi-lateral neck node dissection, those who had bi-lateral neck node dissection had a significantly greater percentage of midline reaching and midline crossing tumours ($p<0.0001$). There were no age or gender disparities among the group, and there was a greater male preponderance (Table 2). Twelve individuals in all were found to have pN0, and eighty-seven patients had pathological ipsilateral node metastases. Pathological contralateral neck node metastases has only been detected in one case (Table 2). Although it did not reach statistical significance, OPC patients having ipsilateral neck node dissection had a superior overall survival (OS) of 54 months compared to individuals who had bi-lateral neck node dissection (51 months). Ipsi-lateral neck node dissection had a much-improved RFS compared to patients with bi-lateral neck node dissection.

Preoperative and postoperative assessment of the Neck node status in OC and OPC

Clinical examination, CT, or MRI imaging were used to determine lymph node status and the primary tumour location. Only three individuals out of two hundred patients were diagnosed with bi-lateral pathological node metastasis (pN+), 178 patients with ipsi-lateral pathological node metastasis (pN+), and 19 patients with no pathological node metastases (pN0). Every patient has contralateral N0 status on radiological imaging and in the clinical examination during the preoperative evaluation.

Discussion

For oral and oropharyngeal squamous cell carcinoma (SCC), the most important prognostic factor at the time of diagnosis is the existence of metastases to cervical lymph nodes[6]. Currently, there isn't

Table 1: Clinico-pathological characteristics in oral cancer patients

Parameters		Ipsilateral ND (100)	Contralateral ND (100)	P value
Age (years)		50 ± 6.48	49.68 ± 7.26	0.98
Gender	Male	72	76	0.66
	Female	28	24	
Location	Cheek (Buccal mucosa)	23	19	0.06
	Bucco alveolar sulcus	11	17	
	Mouth floor	15	30	
	Tongue	51	34	
Laterality	Lateral	82	51	<0.0001
	Mid-line reaching	16	25	
	Mid-line crossing	2	24	
pT status	T3	90	88	0.23
	T4	10	12	
pN-status	None (N0)	07	0	0.11
	Ipsilateral (N+)	93	98	
	Bilateral (N+)	0	2	
Grading	G1	12	18	0.21
	G2	56	64	
	G3	30	17	
	G4	2	1	
R-Status	R0	98	97	0.68
	R1	2	3	
	R2	0	0	

Table 2: Clinico-pathological characteristics of oropharyngeal cancer patients

Parameters		Ipsilateral ND (50)	Bilateral ND (50)	P value
Age (years)		48.12 ± 5.76	49.68 ± 4.93	0.72
Gender	Male	37	39	0.65
	Female	13	11	
Location	Tonsil	2	3	<0.05
	Soft Palate + Hard Palate	13+17	14+13	
	Tongue Base	18	20	
Laterality	Lateral	42	25	<0.0001
	Mid-line reaching	6	11	
	Mid-line crossing	2	14	
pT status	T3	47	40	<0.05
	T4	3	10	
pN-status	None (N0)	08	04	<0.05
	Ipsilateral (N+)	42	45	
	Bilateral (N+)	0	1	
Grading	G1	2	3	0.76
	G2	21	20	
	G3	25	27	
	G4	1	0	
R-Status	R0	48	46	0.81
	R1	2	4	
	R3	0	0	

a widely recognized gold standard for evaluating lymph node involvement prior to therapy in cases of oral cancer (OC) and oropharyngeal cancer (OPC).

Occult metastases have been found in 20–44% of individuals in studies on OC and OPC individuals having clinically negative necks[7]. The current approach is to propose elective neck dissection (END) for most patients who arrive with clinically negative necks, as there is consensus that END is required when the chance of hidden metastases surpasses 15–20%.

There has been much discussion on the use of END in patients with OC/OP squamous cell cancer. This is due to worries about possible overtreatment because, independent of lesion size, cervical node status, or recurrence treatment method, salvage rates for regional recurrent disease are noticeably low, especially in early-stage patients[18]. Significantly better overall survival (OS) and recurrence-free survival (RFS) were seen by D'Cruz et al. following ipsilateral END in comparison to untreated peers[14].

The choice to execute END in the contralateral node-negative neck, however, is still up for debate. The oncological results of ipsilateral and bilateral neck dissections performed on OPC/OC patients who had contralateral N0 neck are examined in this research. Clinically node-negative necks can be treated with END, postoperative radiation, or "wait and scan" methods. However, there are noticeably few prospective trials that compare scan and wait,

elective neck dissection, and contralateral radiation, among contralateral node-negative patients.

Contralateral neck metastasis (N2c) in OC and OPC has a poor prognosis that is similar to ipsilateral metastasis (N2b). According to published research, the incidence of occult contralateral metastasis in OC and OPC is estimated to be between 4 to 16%[16,17]. Tumour size and midline position are known to increase the risk of this condition[15,19]. For midline-reaching/crossing tumours and tumours staged T2 and higher, recommendations have been made for END of the contralateral cN0 neck; however, it is uncertain if this procedure is superior than radiation in terms of OS or RFS[19]. Studies that have already been conducted, such the one by Olzowy et al., have shed light on the prevalence of contralateral neck metastases but have not yet produced sufficient data to determine if END is more beneficial than radiation treatment[19].

Furthermore, improvements in imaging technologies more especially, DWI (diffusion-weighted imaging) in MRI—have greatly improved the precision of determining involvement of lymph node[20]. Ultrasonography has higher diagnostic sensitivity, as evidenced by recent research comparing its diagnostic accuracy with CT/(18)F-FDG-PET and DWI with fused (18)F-FDG-PET-MR images[21]. However, there is disagreement on the usefulness CT scan of head and neck in detecting metastasis of occult lymph node, with reported sensitivities ranging from 48 to 100%[22,23]. The current series found a small but statistically significant over-staging of N-status, which was mostly caused by the pre-therapeutic combination of the lymph node basin MRI and CT images.

Remarkably, three patients that is, 01% of the whole group and 02% of those who had contralateral END surgery had occult contralateral lymph node metastases. There were no variations in RFS and OS of newly diagnose cases of OC and OPC, having ipsilateral or bi-lateral neck dissection.

These results imply that individuals identified with contralateral N0 neck after a combination of MRI/CT scans and clinically N0 status may benefit from the omission of contralateral END in OC/OPC. To fully assess possible surgical therapeutic de-escalation, however, prospective randomised studies are required in order to draw firm findings.

Conclusion

The primary discovery of this study is that in patients with newly diagnose cases of oral and oropharyngeal squamous cell carcinoma (SCC) with contra-lateral N0 neck node status, bilateral neck dissection of N0 contralateral neck did not increase OS or RFS. It is necessary to examine wait and scan as a feasible strategy in contra-lateral node-negative necks through prospective clinical studies.

References

1. Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, Jemal A. Global cancer statistics, 2012. CA: a cancer journal for clinicians. 2015;65(2):87–108. Available from: https://doi.org/10.3322/caac.21262.
2. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. A Cancer Journal for Clinicians. 2021;71(3):209–249. Available from: https://doi.org/10.3322/caac.21660.
3. Gormley M, Creaney G, Schache A, Ingarfield K, Conway DI. Reviewing the epidemiology of head and neck cancer: Definitions, trends and risk factors. British Dental Journal . 2022;233:780–786. Available from: https://doi.org/10.1038/s41415-022-5166-x.
4. Jacobi C, Ayx I, Fritsche K, Piontek G, Hoffmann D, Weirich G, et al. Potential impact of human papilloma virus on survival of basaloid squamous carcinoma of the head and neck. Oncotarget. 2015;6(5):3462–3470. Available from: https://doi.org/10.18632/oncotarget.3062.
5. Haigentz M, Hartl DM, Silver CE, Langendijk JA, Strojan P, Paleri V. Distant metastases from head and neck squamous cell carcinoma. Part III. Treatment. Oral Oncology. 2012;48(9):787–793. Available from: https://doi.org/10.1016/j.oraloncology.2012.03.019.
6. Snow GB, Van Den Brekel MW, Leemans CR, Patel P. Surgical management of cervical lymph nodes in patients with oral and oropharyngeal cancer. Recent Results in Cancer Research. 1994;134:43–55. Available from: https://doi.org/10.1007/978-3-642-84971-8_6.
7. Shah JP. Patterns of cervical lymph node metastasis from squamous carcinomas of the upper aerodigestive tract. American Journal of Surgery. 1990;160(4):405–409. Available from: https://doi.org/10.1016/s0002-9610(05)80554-9.
8. Lim YC, Koo BS, Lee JS, Lim JY, Choi EC. Distributions of cervical lymph node metastases in oropharyngeal carcinoma: therapeutic implications for the N0 neck. Laryngoscope. 2006;116(7):1148–1152. Available from: https://doi.org/10.1097/01.mlg.0000217543.40027.1d.
9. Simental AA, Duvvuri U, Johnson JT, Myers EN. Selective neck dissection in patients with upper aerodigestive tract cancer with clinically positive nodal

disease. Annals of Otology, Rhinology & Laryngology. 2006;115(11):846–849. Available from: https://doi.org/10.1177/000348940611501109.
10. de Oliveira Santos AB, Cernea CR, Inoue M, Ferraz AR. Selective neck dissection for node-positive necks in patients with head and neck squamous cell carcinoma: a word of caution. Archives of otolaryngology-head & neck surgery. 2006;132(1):79–81. Available from: https://doi.org/10.1001/archotol.132.1.79.
11. Andersen PE, Warren F, Spiro J, Burningham A, Wong R, Wax MK, et al. Results of selective neck dissection in management of the node-positive neck. Archives of otolaryngology-head & neck surgery. 2002;128(10):1180–1184. Available from: https://doi.org/10.1001/archotol.128.10.1180.
12. Haddadin KJ, Soutar DS, Oliver RJ, Webster MH, Robertson AG, MacDonald DG. Improved survival for patients with clinically T1/T2, N0 tongue tumors undergoing a prophylactic neck dissection. Head Neck. 1999;21(6):517–525. Available from: https://doi.org/10.1002/(sici)1097-0347(199909)21:6%3C517::aid-hed4%3E3.0.co;2-c.
13. Capote A, Escorial V, Muñoz-Guerra MF, Rodríguez-Campo FJ, Gamallo C, Naval L. Elective neck dissection in early-stage oral squamous cell carcinoma-does it influence recurrence and survival. Head Neck. 2007;29(1):3–11. Available from: https://doi.org/10.1002/hed.20482.
14. D'Cruz AK, Vaish R, Kapre N, Dandekar M, Gupta S, Hawaldar R, et al. Elective versus Therapeutic Neck Dissection in Node-Negative Oral Cancer. New England Journal of Medicine. 2015;373:521–529. Available from: https://www.nejm.org/doi/full/10.1056/NEJMoa1506007.
15. Olzowy B, Tsalemchuk Y, Schotten KJ, Reichel O. Frequency of bilateral cervical metastases in oropharyngeal squamous cell carcinoma: a retrospective analysis of 352 cases after bilateral neck dissection. Head Neck. 2011;33(2):239–243. Available from: https://doi.org/10.1002/hed.21436.
16. Lim YC, Lee JS, Koo BS, Kim SH, Kim YH, Choi EC. Treatment of contralateral N0 neck in early squamous cell carcinoma of the oral tongue: elective neck dissection versus observation. Laryngoscope. 2006;116(3):461–465. Available from: https://doi.org/10.1097/01.mlg.0000195366.91395.9b.
17. Lim YC, Lee SY, Lim JY, Shin HA, Lee JS, Koo BS, et al. Management of contralateral N0 neck in tonsillar squamous cell carcinoma. Laryngoscope. 2005;115(9):1672–1675. Available from: https://doi.org/10.1097/01.mlg.0000184791.68804.0b.
18. Kaya S, Yilmaz T, Gürsel B, Saraç S, Sennaroğlu L. The value of elective neck dissection in treatment of cancer of the tongue. American journal of otolaryngology. 2001;22(1):59–64. Available from: https://doi.org/10.1053/ajot.2001.20681.
19. Kowalski LP, Bagietto R, Lara JR, Santos RL, Tagawa EK, Santos IR. Factors influencing contralateral lymph node metastasis from oral carcinoma. Head Neck. 1999;21(2):104–110. Available from: https://doi.org/10.1002/(sici)1097-0347(199903)21:2%3C104::aid-hed2%3E3.0.co;2-l.
20. Suh CH, Choi YJ, Baek JH, Lee JH. The Diagnostic Value of Diffusion-Weighted Imaging in Differentiating Metastatic Lymph Nodes of Head and Neck Squamous Cell Carcinoma: A Systematic Review and Meta-Analysis. American Journal of Neuroradiology. 2018;39(10):1889–1895. Available from: https://doi.org/10.3174/ajnr.A5813.
21. Heusch P, Sproll C, Buchbender C, Rieser E, Terjung J, Antke C, et al. Diagnostic accuracy of ultrasound, 18F-FDG-PET/CT, and fused 18F-FDG-PET-MR images with DWI for the detection of cervical lymph node metastases of HNSCC. Clinical Oral Investigations. 2014;18(3):969–978. Available from: https://dx.doi.org/10.1007/s00784-013-1050-z.
22. Knopf A, Jacob S, Bier H, Scherer EQ. Bilateral versus ipsilateral neck dissection in oral and oropharyngeal cancer with contralateral cN0 neck. European Archives of Oto-Rhino-Laryngology. 2020;277(11):3161–3168. Available from: https://dx.doi.org/10.1007/s00405-020-06043-2.
23. Mazzawi E, El-naaj IA, Ghantous Y, Balan S, Sabo E, Rachmiel A, et al. Clinical significance of preoperative imaging in oral squamous cell carcinoma compared with lymph node status: a comparative retrospective study. Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology. 2018;125(5):423–430. Available from: https://dx.doi.org/10.1016/j.oooo.2017.11.021.

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