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Extracapsular extension in oral cavity cancers—predictive factors and impact on recurrence pattern and survival

S. K. Rajappa[1], U. Maheshwari[2], D. Ram[1], V. P. B. Koyyala[2], G. Mandal[1], R. Kumar[1], A. K. Dewan[1], G. Vishwakarma[3]

[1]Department of Surgical Oncology, Rajiv Gandhi Cancer Institute and Research Centre, New Delhi, India; [2]Department of Medical Oncology, Rajiv Gandhi Cancer Institute and Research Centre, New Delhi, India; [3]Department of Statistics and Research Analysis, Rajiv Gandhi Cancer Institute and Research Centre, New Delhi, India

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Abstract. Extracapsular extension (ECE) has long been considered a poor prognostic factor in oral cavity cancer, the presence of which warrants intensification of adjuvant therapy. This study was done to analyze the survival of patients with ECE who received adjuvant chemoradiation. Patients with pathologically confirmed squamous cell carcinoma of the oral cavity, with a minimum of 2 years of follow-up, who were treated at a tertiary cancer centre in New Delhi, India during the years 2009–2017, were included. On multivariate analysis, ECE was significantly associated with depth of invasion >10 mm and tumour deposit size >5 mm. Among the node-positive group, patients without ECE had a 5-year disease-free survival (DFS) and 5-year overall survival (OS) advantage over ECE-positive patients of 7.8% (63.8% vs. 56.0%) and 16.5% (87.2% vs. 70.7%), respectively. For patients with ECE, the hazard ratio for DFS and OS was 1.3 (95% confidence interval 0.97–1.75, P = 0.078) and 2.30 (95% confidence interval 1.35–3.92, P = 0.002), respectively. ECE remains one of the strongest predictors of recurrence and survival in oral cancer patients, and despite aggressive adjuvant therapy, distant recurrence is still significantly high.

Key words: oral cancer; extracapsular extension; adjuvant therapy; survival; chemoradiation.

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''Oral cancers, an Indian pandemic'' is what authors are calling the recent worrisome rise in the incidence of oral cancer in India[1]. The National Cancer Registry Programme has reported this rise in upper aerodigestive tract malignancies in both sexes[2]. Tobacco use is the major aetiological factor, and the Global Adult Tobacco Survey (GATS) conducted in 2009–10 indicated that 34.6% of adults (47.9% of males and 20.3% of females) were current tobacco users[3]. Oral cancer thus constitutes a major health burden in India, and identifying prognostic factors associated with oral cancers has become an important initial step in management. Lymph node metastasis in head and neck cancers is a well-known clinical and pathological prognostic factor leading to worse survival[4,5]. In patients with nodal positivity, extracapsular spread confers worse surviv-

al; this was first described by Bennett et al. in 1971[6]. Furthermore, various studies have shown that node-positive patients with extracapsular extension (ECE) have even worse survival than node-negative patients with ECE[7,8].

The decision to add chemotherapy to radiotherapy as adjuvant treatment in patients with ECE was based on the landmark studies by Bernier et al. and Cooper et al.[9–11]. The importance of ECE in head and neck cancers was considered in the recent eighth edition of the American Joint Committee on Cancer (AJCC) Cancer Staging Manual, and ECE was incorporated in the TNM staging guidelines[12,13]. The prognosis of ECE-positive patients remains grim despite the use of trimodality treatment, and some studies have suggested that irrespective of prognostic factors, a third of the patients will experience recurrence even after adjuvant therapy[14]. The aim of this study was to observe the effects of ECE on survival in oral cancer patients and to look for pathological predictive factors for ECE.

Methods

A retrospective analysis of histopathologically confirmed oral cancer was conducted at Rajiv Gandhi Cancer Institute and Research Centre, a tertiary care cancer hospital in India. All oral cancer patients registered at the centre during the time period of 2009–2017 were considered. Clinical and histopathological data were extracted from the electronic medical records. Only patients with a squamous cell histology and those with a minimum follow-up of 2 years, or who were followed up until death, were included in this analysis. Patients with upfront metastatic disease and those who defaulted treatment were excluded from the study. A total of 1431 patients were included in the cohort. ECE positivity was considered if there was an extension of metastatic carcinoma through the fibrous capsule of the lymph node into the surrounding connective tissue. Adjuvant chemoradiation was given to all patients with ECE and positive margins.

Statistical analysis

Descriptive summaries are presented as the mean and standard deviation (SD) or median with range for continuous variables and as frequencies with percentages for categorical variables. The two-sample Z-test for proportions was performed using MedCalc software version 18.5 (MedCalc Software bvba, Ostend, Belgium) to determine the significance for recurrences between the ECE positive and negative groups. The distribution of clinical and pathological factors in the ECE positive and negative groups was tested by cross-tabulation and significance was tested by χ^2 test. Multiple logistic regression was used to predict ECE based on various clinical and pathological factors. The results of the univariate and multivariate analyses are presented as the odds ratio (OR) and 95% confidence interval (CI). The survival analysis was performed using the Kaplan–Meier method and Cox regression analysis, and the log-rank test was used to compare the difference in survival between two factors. A P-value of <0.05 was considered statistically significant. IBM SPSS Statistics version 23.0 (IBM Corp., Armonk, NY, USA) was used for the statistical analysis.

Results

The mean age of the cohort was 49 ± 12.4 (range 22–93) years, and the male to female ratio was 5.2:1. Tobacco chewing was reported by 71.0% of patients. Lymph node positivity was seen in 32.6% of the patients and ECE was present in 14.3% of the whole cohort. The demographic characteristics and tumour characteristics of the study cohort are described in Table 1.

The distribution of patients in the ECE-positive group did not differ significantly from that of the ECE-negative group with respect to sex, tobacco chewing, or comorbidities; however the distribution of patients in the two groups differed significantly with respect to T and N stage (AJCC Cancer Staging Manual seventh edition), lymphovascular invasion (LVI), perineural invasion (PNI), depth of invasion (DOI), and tumour deposit size after adjustment by Bonferroni correction (Table 2).

Logistic regression was applied to identify predictive factors for ECE. The results of the univariate and multivariate analyses for factors predicting ECE are given in Table 3. On univariate analysis, LVI, PNI, DOI >10 mm, and tumour deposit size >5 mm were significantly associated with ECE, with the maximum OR for tumour deposit size in the lymph nodes >5 mm. On multivariate analysis, ECE was significantly associated with DOI >10 mm and tumour deposit >5 mm, and there was a trend towards significance for LVI (Table 3).

Patients with negative lymph node involvement had an absolute 5-year disease-free survival (DFS) and 5-year overall survival (OS) advantage over lymph node-positive patients of 19.8% (80.2% vs. 60.4%) and 11.8% (93.1% vs. 81.3%), respectively. For lymph node-positive patients, the hazard ratio (HR)

Table 1. Demographic profile of the study patients ($N = 1431$).

Variables	*n* (%)[a]
Age, mean ± SD (range)	49 ± 12.4 (22–93)
Sex	
Male	1201 (83.9%)
Female	230 (16.1%)
Smoking	386 (27.0%)
Tobacco use	1016 (71.0%)
Duration of complaints (months), median (range)	3 (1–23)
Grade[b]	
1	105 (7.3%)
2	1296 (90.7%)
3	28 (2.0%)
Lymph node positive	466 (32.6%)
Perineural invasion	303 (21.2%)
Lymphovascular invasion	505 (35.3%)
Adjuvant therapy	
No	460 (32.1%)
RT	740 (51.7%)
CT/RT	231 (16.1%)
Extracapsular extension	
Yes	205 (14.3%)
No	1226 (85.7%)
Follow-up (months), median (range)	40 (39.5–40.5)

RT, radiotherapy; CT, chemotherapy.

[a] Data are presented as the number and percentage of the total study population ($N = 1431$), unless stated otherwise.

[b] Data for grade missing for two patients.

Table 2. Distribution of patients in extracapsular extension positive and negative groups ($N=466$).

	Extracapsular extension		*P*-value
	Positive	Negative	
Sex			
Male	175	231	0.269
Female	30	31	
Smoking			
Yes	58	80	0.610
No	147	181	
Tobacco use			
Yes	155	189	0.459
No	50	72	
Comorbidities			
Yes	94	122	0.852
No	111	139	
T stage[a]			
1	29	57	0.005
2	108	144	
3	20	19	
4	48	41	
N stage[a]			
1	55	159	<0.001
2	150	102	
Perineural invasion			
Yes	130	131	0.005
No	75	130	
Lymphovascular invasion			
Yes	125	112	<0.001
No	80	149	
Depth of invasion (mm)			
<5	25	51	<0.001
6–10	69	121	
>10	111	89	
Mean size of the deposit in the node (mm)			
<5	10	84	<0.001
>5	195	177	
Median tumour deposit size (mm)	13	8	<0.001

[a] According to the seventh edition of the American Joint Committee on Cancer (AJCC) Cancer Staging Manual.

Table 3. Logistic regression analysis for factors predicting extracapsular extension.

Prognostic factor	Univariate analysis			Multivariate analysis		
	OR	95% CI	P-value	OR	95% CI	P-value
Age (years)						
≤45	1					
>45	0.92	0.64–1.33	0.673			
Sex						
Male	1					
Female	0.73	0.43–1.25	0.250			
Tobacco use						
Absent	1					
Present	1.18	0.78–1.79	0.436			
Lymphovascular invasion						
Absent	1			1		
Present	2.08	1.43–3.02	<0.001	1.53	0.99–2.36	0.053
Perineural invasion						
Absent	1			1		
Present	1.72	1.18–2.50	0.004	1.40	0.92–2.13	0.122
Depth of invasion (mm)						
≤10	1			1		
>10	2.28	1.57–3.32	<0.001	1.87	1.23–2.83	0.003
Tumour deposit (mm)						
≤5	1			1		
>5	9.25	4.66–18.39	<0.001	8.66	4.32–17.35	<0.001

OR, odds ratio; CI, confidence interval.

for DFS and OS was 2.36 (95% CI 1.92–2.89, $P < 0.001$) and 2.56 (95% CI 1.77–3.79, $P < 0.001$), respectively. In the node-positive group, patients without ECE had a 5-year DFS and 5-year OS advantage over patients with ECE of 7.8% (63.8% vs. 56.0%) and 16.5% (87.2% vs. 70.7%), respectively. For patients with ECE, the HR for DFS and OS was 1.3 (95% CI 0.97–1.75, $P = 0.078$) and 2.30 (95% CI 1.35–3.92, $P = 0.002$), respectively. Kaplan–Meier curves depicting the survival difference are shown in Figs 1 and 2.

Disease recurrence (local/distant) was seen in 359 of the 1431 patients (25.1%), and 179 of these patients had node-positive disease. In the node-positive group of patients, 87/205 (42.4%) patients with ECE had recurrence as compared to 92/261 (35.2%) without ECE (7.2%, 95% CI 1.63–16.02, $P = 0.11$). Distant recurrence was seen in 34/205 (16.5%) ECE-positive patients and in 23/261 (8.8%) patients without ECE (distant 7.8%, 95% CI 1.67–14.07, $P = 0.011$). Amongst the patients who had disease recurrence, 53.2% (191/359) were alive with disease at the time of analysis.

Discussion

Numerous factors affect the prognosis in oral cancer, and nodal metastasis remains one of the most significant factors affecting survival[15]. ECE was first described by Willis in 1930 in their study entitled ''Epidermoid carcinoma of the head and neck, with special reference to metastasis''[16]. ECE was later confirmed to be associated with worse survival in various studies[17–19]. Furthermore, some researchers have observed that ECE affects regional and distant recurrence[20]. Lymph node metastasis in head and neck cancers has been reported to occur in about 28% of patients[21,22]; in the present study, this was seen in 32.6% of patients. ECE, as observed in various studies, is seen in about 60% of lymph node-positive patients[22–24], and was seen in 44.0% (205/466) of lymph node-positive patients in the present study.

ECE is defined as the extension of metastatic carcinoma through the fibrous capsule of the lymph node into surrounding connective tissue[13], however the definition is not standard and inter-observer variability and discrepancy between pathological examination and actual ECE positivity has been observed in a few studies[25,26]. Various pathological factors have been found to be associated with ECE and these associations have become an important aid to the pathologist. These

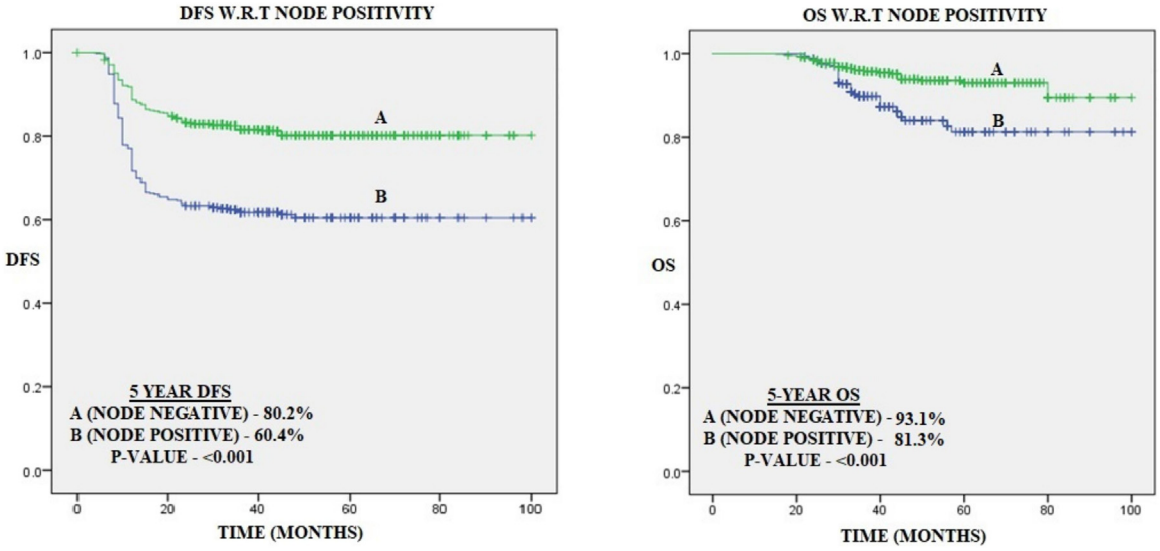

Fig. 1. Kaplan–Meier survival curves for 5-year disease-free survival (DFS) and 5-year overall survival (OS) in relation to node positivity.

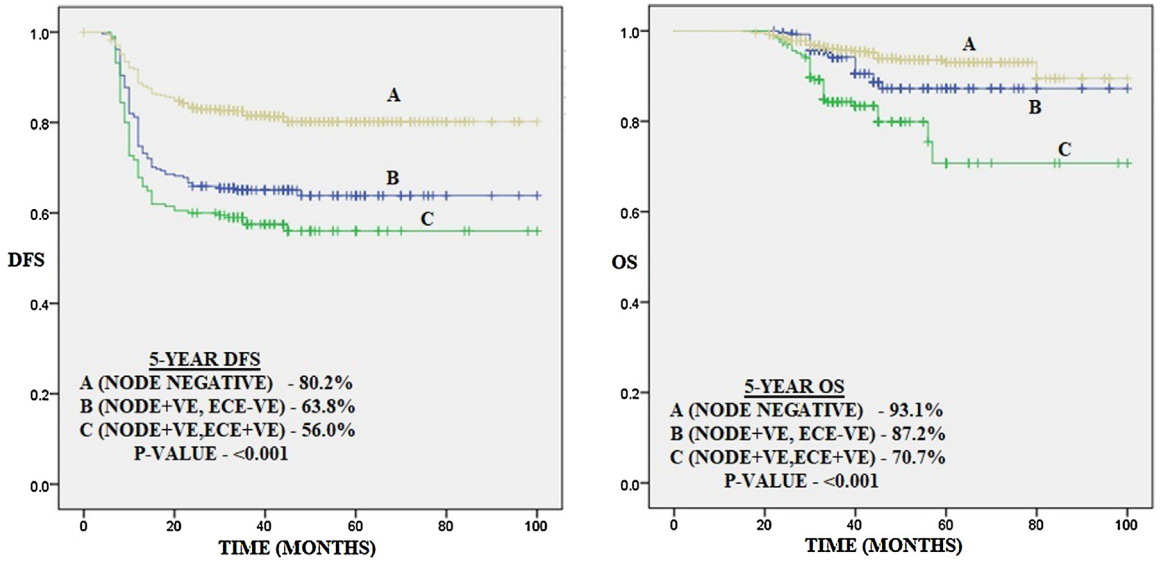

Fig. 2. Kaplan–Meier survival curves for 5-year disease-free survival (DFS) and 5-year overall survival (OS) in relation to extracapsular extension (ECE).

factors can act as adjunctive findings to decide on the ECE status, thus leading to reduced inter-observer variability.

Mair et al. evaluated factors associated with ECE in early oral cavity cancers[22]. A tumour thickness >5 mm and tumour deposit size in the lymph node >15 mm were significantly associated with ECE on multivariate analysis[22]. In the present study, ECE was found to be strongly associated with a tumour deposit size >5 mm and DOI > 10 mm.

LVI has long been postulated to be an important prognostic factor and the presence of LVI can be considered an initial first step in the development of nodal or distant metastasis[27]. Adel et al. observed a significant association of LVI with ECE on multivariate analysis, with an OR of 1.83 (P = 0.007)[28]. In the present study, a trend towards a significant association of ECE with LVI was observed on multivariate analysis, with an HR of 1.53 (95% CI 0.99–2.36, P = 0.053). The tumour deposit size in the lymph node was found to have the strongest association with ECE, with a OR of 8.66 (95% CI 4.32–17.35, P < 0.001).

Since occult micrometastatic ECE may be present in 10.5–25% of clinically node-negative patients[20], identifying factors strongly associated with ECE becomes important. It is also proposed that the presence of ECE is underestimated, as the current techniques of pathological examination may miss microinvasions of the capsule[20] and nodal metastasis of <2 mm can also be associated with ECE[29]. Diagnosing ECE is also important as it is one of the two main factors in the decision to add chemotherapy to adjuvant radiotherapy, with the other factor being positive margins[9–11].

Mair et al. observed a 3-year DFS of 82%, 63%, and 57.5% (P = 0.001) for

node-negative, node-positive without ECE, and node-positive with ECE, respectively[22]. Similarly, Maxwell et al. reported a 3-year disease-specific survival of 45% vs. 71% (P = 0.0018) for ECE-positive vs. ECE-negative groups, respectively[30]. In the present study, a 5-year DFS of 80.2%, 63.8%, and 56.0% was observed for node-negative, node-positive without ECE, and node-positive with ECE, respectively. Other studies have reported 5-year OS in lymph node-positive patients ranging from 58% to 60%[31,32]. Mair et al. observed 3-year OS of 84.4%, 68.5%, and 59.2% in patients with lymph node-negative, lymph node-positive without ECE, and lymph node-positive with ECE, respectively[22]. In the present study, 5-year OS was 87.2% for lymph node-positive without ECE vs. 70.7% for lymph node-positive with ECE. Other studies including all head and neck cancers have reported lower 5-year survival rates than those observed in the present study, ranging from 35% to 48% in lymph node-positive patients with ECE[18,33,34].

The reasons for the differences between studies could be that out of the total patients with tumour recurrences in the present study, 53.2% were alive with disease at the time of analysis, of whom 58.1% were in the node-positive group, and most of these patients were on palliative chemotherapy or best supportive care. Furthermore, the mean age of the cohort was 49 years, representing a younger population when compared to other studies. Also, two or more associated comorbidities were seen in only 9.5% of patients, and 48.0% of patients had no comorbidities. Lastly, in the present study it was observed that distant recurrences occurred more commonly in the ECE-positive group than in the ECE-negative group (P = 0.011). This observation corroborates the results of the meta-analysis by Mermod et al., who found distant metastasis to be significantly associated with ECE with an OR of 2.18 (95% CI 1.23–3.87)[35].

Further studies are required to investigate other therapeutic options, and questions of maintenance therapy in these high-risk patients need to be answered soon. Strengths of this study include the long median follow-up time of the patients and the number of patients included. This appears to be one of the largest cohorts studied to predict the risk factors for ECE. The main drawbacks of this study are the retrospective nature and the fact that the pathological analysis was not done by a single pathologist, which brings inter-observer variability. This study did not analyse microinvasion of the capsule and its impact on survival.

In conclusion, ECE remains one of the strongest predictors of recurrence and survival in oral cancer patients, and the presence of ECE merits intensification of adjuvant therapy. Pathological factors associated with ECE on multivariate analysis were depth of invasion >10 mm and tumour deposit size >5 mm, and there was a trend towards significance for lymphovascular invasion. The authors believe that there is scope for improvements in adjuvant therapeutic options for patients with ECE to decrease distant metastasis rates.

Patient consent

Not required.

Funding

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Ethical approval

As this was a retrospective study, the institutional review board exempted approval.

Competing interests

None.

References

1. Gupta B, Johnson NW. Oral cancer: Indian pandemic. *Br Dent J* 2017;(222):497.
2. Katoch VM. *Three-year report of population based cancer registries 2012–2014*. Bengaluru, India: National Centre for Disease Informatics and Research –National Cancer Registry Programme; 2016.
3. Ministry of Health and Family Welfare, Government of India; International Institute for Population Sciences, Mumbai, India. Global Adult Tobacco Survey (GATS) India: 2009–2010. http://www.searo.who.int/tobacco/documents/2010-pub2.pdf [Accessibility verified March 22, 2019].
4. Gil Z, Carlson DL, Boyle JO, Kraus DH, Shah JP, Shaha AR, Singh B, Wong RJ, Patel SG. Lymph node density is a significant predictor of outcome in patients with oral cancer. *Cancer* 2009;**115**:5700–10.
5. Kowalski LP, Bagietto R, Lara JR, Santos RL, Silva JF, Magrin J. Prognostic significance of the distribution of neck node metastasis from oral carcinoma. *Head Neck* 2000;**22**:207–14.
6. Bennett SH, Futrell JW, Roth JA, Hoye RC, Ketcham AS. Prognostic significance of histologic host response in cancer of the larynx or hypopharynx. *Cancer* 1971;**28**:1255–65.
7. Ferlito A, Rinaldo A, Devaney KO, MacLennan K, Myers JN, Petruzzelli GJ, Shaha AR, Genden EM, Johnson JT, de Carvalho MB, Myers EN. Prognostic significance of microscopic and macroscopic extracapsular spread from metastatic tumor in the cervical lymph nodes. *Oral Oncol* 2002;**38**:747–51.
8. Puri SK, Fan CY, Hanna E. Significance of extracapsular lymph node metastases in patients with head and neck squamous cell carcinoma. *Curr Opin Otolaryngol Head Neck Surg* 2003;**11**:119–23.
9. Bernier J, Domenge C, Ozsahin M, Matuszewska K, Lefebvre JL, Greiner RH, Giralt J, Maingon P, Rolland F, Bolla M, Cognetti F, Bourhis J, Kirkpatrick A, van Glabekke M. Postoperative irradiation with or without concomitant chemotherapy for locally advanced head and neck cancer. *N Engl J Med* 2004;**350**:1945–52.
10. Cooper JS, Pajak TF, Forastiere AA, Jacobs J, Campbell BH, Saxman SB, Kish JA, Kim HE, Cmelak AJ, Rotman M, Machtay M, Ensley JF, Chao KS, Schultz CJ, Lee N, Fu KK. Postoperative concurrent radiotherapy and chemotherapy for high-risk squamous cell carcinoma of the head and neck. *N Engl J Med* 2004;**350**:1937–44.
11. Bernier J, Cooper JS, Pajak TF, van Glabbeke M, Bourhis J, Forastiere A, Ozsahin EM, Jacobs JR, Jassem J, Ang KK, Lefèbvre JL. Defining risk levels in locally advanced head and neck cancers: a comparative analysis of concurrent postoperative radiation plus chemotherapy trials of the EORTC (#22931) and RTOG (#9501). *Head Neck* 2005;**27**:843–50.
12. Amin MB, Greene FL, Edge SB, Compton CC, Gershenwald JE, Brookland RK, Meyer L, Gress DM, Byrd DR, Winchester DP. The eighth edition AJCC Cancer Staging Manual: continuing to build a bridge from a population-based to a more "personalized" approach to cancer staging. *CA Cancer J Clin* 2017;**67**:93–9.
13. Lydiatt WM, Patel SG, O'Sullivan B, Brandwein MS, Ridge JA, Migliacci JC, Loomis AM, Shah JP. Head and neck cancers—major changes in the American Joint Committee on Cancer eighth edition Cancer Staging Manual. *CA Cancer J Clin* 2017;**67**:122–37.
14. Greenberg JS, El Naggar AK, Mo V, Roberts D, Myers JN. Disparity in pathologic and clinical lymph node staging in oral tongue carcinoma. Implication for therapeutic decision making. *Cancer* 2003;**98**:508–15.
15. Cho JK, Hyun SH, Choi N, Kim MJ, Padera TP, Choi JY, Jeong HS. Significance of lymph node metastasis in cancer dissemination of head and neck cancer. *Transl Oncol* 2015;**8**:119–25.
16. Willis RA. Epidermoid carcinoma of the head and neck, with special reference to metastasis. *J Pathol* 1930;**33**:501–26.
17. Carter RL, Barr LC, O'Brien CJ, Soo KC, Shaw HJ. Transcapsular spread of metastatic

squamous cell carcinoma from cervical lymph nodes. *Am J Surg* 1985;**150**:495–9.
18. Myers JN, Greenberg JS, Mo V, Roberts D. Extracapsular spread. A significant predictor of treatment failure in patients with squamous cell carcinoma of the tongue. *Cancer* 2001;**92**:3030–6.
19. Suton P, Salaric I, Granic M, Mueller D, Luksic I. Prognostic significance of extracapsular spread of lymph node metastasis from oral squamous cell carcinoma in the clinically negative neck. *Int J Oral Maxillofac Surg* 2017;**46**:669–75.
20. Coatesworth AP, MacLennan K. Squamous cell carcinoma of the upper aerodigestive tract: the prevalence of microscopic extracapsular spread and soft tissue deposits in the clinically N0 neck. *Head Neck* 2002;**24**:258–61.
21. El-Naaj IA, Leiser Y, Shveis M, Sabo E, Peled M. Incidence of oral cancer occult metastasis and survival of T1–T2N0 oral cancer patients. *J Oral Maxillofac Surg* 2011;**69**:2674–9.
22. Mair MD, Shetty R, Nair D, Mathur Y, Nair S, Deshmukh A, Thiagarajan S, Pantvaidya G, Lashkar S, Prabhash K, Chaukar D, Pai P, Cruz AD, Chaturvedi P. Depth of invasion, size and number of metastatic nodes predicts extracapsular spread in early oral cancers with occult metastases. *Oral Oncol* 2018;**81**:95–9.
23. Johnson JT, Barnes EL, Myers EN, Schramm VL, Borochovitz D, Sigler BA. The extracapsular spread of tumors in cervical node metastasis. *Arch Otolaryngol* 1981;**107**:725–9.
24. Johnson JT, Myers EN, Bedetti CD, Barnes EL, Schramm VL, Thearle PB. Cervical lymph node metastases. *Arch Otolaryngol* 1985;**111**:534–7.
25. Brannan AG, Johnstone PA, Cooper J. Extracapsular tumor extension in cervical lymph nodes: reconciling the literature and SEER data. *Head Neck* 2011;**33**:525–8.
26. Van den Brekel MW, Lodder WL, Stel HV, Bloemena E, Leemans CR, van der Waal I. Observer variation in the histopathologic assessment of extranodal tumor spread in lymph node metastases in the neck. *Head Neck* 2012;**34**:840–5.
27. Jakobsson PA, Eneroth CM, Killander D, Moberger G, Mårtensson B. Histologic classification and grading of malignancy in carcinoma of the larynx. *Acta Radiol Ther Phys Biol* 1973;**12**:1–8.
28. Adel M, Kao HK, Hsu CL, Huang JJ, Lee LY, Huang Y, Browne T, Tsang NM, Chang YL, Chang KP. Evaluation of lymphatic and vascular invasion in relation to clinicopathological factors and treatment outcome in oral cavity squamous cell carcinoma. *Medicine (Baltimore)* 2015;**94**:e1510.
29. Don DM, Calcaterra TC, Anzai Y, Lufkin RB, Fu YS. Evaluation of cervical lymph node metastases in squamous cell carcinoma of the head and neck. *Laryngoscope* 1995;**105**:669–74.
30. Maxwell JH, Ferris RL, Gooding W, Cunningham D, Mehta V, Kim S, Myers EN, Johnson J, Chiosea S. Extracapsular spread in head and neck carcinoma: impact of site and human papillomavirus status. *Cancer* 2013;**119**:3302–8.
31. Chandu A, Adams G, Smith AC. Factors affecting survival in patients with oral cancer: an Australian perspective. *Int J Oral Maxillofac Surg* 2005;**34**:514–20.
32. Kim BG, Kim JH, Kim MI, Han JJ, Jung S, Kook MS, Park HJ, Ryu SY, Oh HK. Retrospective study on factors affecting the prognosis in oral cancer patients who underwent surgical treatment only. *Maxillofac Plast Reconstr Surg* 2016;**38**:3.
33. Pinsolle J, Pinsolle V, Majoufre C, Duroux S, Demeaux H, Siberchicot F. Prognostic value of histologic findings in neck dissections for squamous cell carcinoma. *Arch Otolaryngol Head Neck Surg* 1997;**123**:145–8.
34. Kapoor C, Vaidya S, Wadhwan V, Malik S. Lymph node metastasis: a bearing on prognosis in squamous cell carcinoma. *Indian J Cancer* 2015;**52**:417–24.
35. Mermod M, Tolstonog G, Simon C, Monnier Y. Extracapsular spread in head and neck squamous cell carcinoma: a systematic review and meta-analysis. *Oral Oncol* 2016;**62**:60–71.

Address:
Suhas Kodasoge Rajappa
Department of Surgical Oncology
Rajiv Gandhi Cancer Institute and Research Centre
New Delhi 110085
India
Tel: +91 8130515661
suhas9490@gmail.com,
udip.the.drift.king@gmail.com,
drdharmapoonia@gmail.com,
pradeepbabu.koyyala@gmail.com,
ghanashyam009@gmail.com,
drrajeevkumar2017@gmail.com,
dewan.ajay@gmail.com,
gayatri@rgcirc.org