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Lymph node staging systems in oral squamous cell carcinoma: A comparative analysis

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ABSTRACT

Objectives: The 8th edition of the AJCC has introduced a new nodal staging system for head and neck cancers. Alternate nodal staging systems exist, however they have not been compared to the current AJCC staging system.
Materials and methods: **A** retrospective analysis of 643 patients with oral squamous cell carcinoma (OSCC) treated with surgery ± adjuvant therapy in a single institution between 2004 and 2014 was undertaken. Nodal staging was performed using AJCC 8th edition (AJCC8), number of positive lymph nodes (PN), log odds of positive lymph nodes (LODDS) and lymph node ratio (LNR). Survival analyses for disease free survival (DFS) and overall survival (OS) were performed with the different staging systems and they were compared on the basis of hazard consistency, hazard discrimination, explained variation and likelihood difference.
Results: Overall, PN and LNR best predicted OS and DFS in our cohort of patients. AJCC8 had poor discrimination between sub-stages of pN2.
Conclusion: PN and LNR provided the most accurate prediction of OS and DFS for patients with OSCC.

Background

Oral squamous cell carcinoma (OSCC) is a major cause of morbidity and mortality globally. Lymph node spread is arguably the single most important prognostic determinant, resulting in a reduction of survival by up to 50% [1]. The lymph nodal staging used is the American Joint Committee on Cancer TNM staging [2], which considers the size of lymph nodes, laterality and number of nodes. In addition, the recent 8th edition of the AJCC introduced a modification in the nodal staging by incorporating extranodal extension (ENE) [3]; those with ENE in nodes smaller than 3 cm are classified as N2a and those larger than 3 cm are classified as N3b. Incorporation of ENE was intended to better prognosticate patients, however some criticisms of the previous AJCC staging system still exist. Questions regarding poor discrimination within stage N2 and doubtful prognostic value of bilateral nodal disease [4] have been raised. Additionally, some authors argue that AJCC pathological staging is limited by the quality of the neck dissection and nodal yield [5].

To address this, several alternative staging systems have been proposed. Lymph node density or lymph node ratio (LNR) - which is the ratio of excised positive lymph nodes to the total number of excised nodes – has been shown as an alternative system that can address some of these shortcomings [6], correlating well with disease free and overall survival. Number of positive lymph nodes (PN) has also been shown to be a more accurate predictor of survival than the AJCC 7th edition TNM staging [7] for oral and oropharyngeal tumours, with number of positive lymph nodes being incorporated into the AJCC 8th edition pathological staging for surgically treated human papilloma virus (HPV) related oropharyngeal cancers [8]. Log odds of positive lymph nodes (LODDS), which is the log of the ratio of positive lymph nodes to the number of negative lymph nodes, has also been described as a sensitive staging system and validated on a large number of patients, with recommendations that it be included in future staging systems [9,10]. However there is limited literature comparing these alternative staging systems with the AJCC 8th edition TNM (AJCC8) staging for OSCC. The purpose of this study was to identify the lymph node staging system which best predicted locoregional control and survival in our cohort of OSCC.

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Materials and methods

Patient population and treatment protocol

From a prospectively maintained database of patients treated at our institution we identified 643 consecutive patients of OSCC (tongue, buccal mucosa, floor of mouth and alveolus) treated between 2004 and 2014. All patients received contrast-enhanced computerised tomography (CT) or magnetic resonance imaging (MRI) of the head and neck and plain CT of the thorax as part of their routine staging workup. Only patients who underwent surgical resection with curative intent in our institution were included in our analysis. All patients were treated with wide excision of the primary lesion (a gross margin of 1–1.5 cm aiming for a minimum microscopic margin of 5 mm) and ipsilateral selective neck dissection, with appropriate reconstruction where required. Contralateral neck dissection was performed for clinically or radiologically positive nodes, lesions crossing the midline or lesions with extensive floor of mouth involvement. Adjuvant radiotherapy was administered for advanced stage (III/IV), any nodal disease, or more than one adverse pathological feature (perineural invasion, lymphovascular invasion, or poor differentiation). Adjuvant chemoradiotherapy was administered for positive/close margins or extranodal extension.

Definitions of survival

Recurrent disease was defined as any proven local, regional or distant disease occurring at least three months after completion of treatment. Overall survival (OS) was defined as time from initial surgery to date of death or last follow-up evaluation. Disease free survival (DFS) was defined as time from initial surgery to date of recurrence, whether local, regional or distant.

Nodal staging system classification

Patients were classified four nodal staging systems based on histopathology: AJCC8, LNR, PN and LODDS. LNR stages were categorized as 0, < 0.1, 0.1–0.4 and > 0.4. A cut-off of 0.1 was used in accordance with previously published studies [11–13]. For number of positive nodes, the stages considered were 0, 1–2, 3–4 and ≥5. This was also in accordance with previously published data [7]. For LODDS, we used the categories ≤ −1.68, −1.68 to < −1.29, −1.29 to −0.88 and > 0.88, which have been described in previous large series [9,10].

Statistical analysis

Continuous data were expressed as mean and standard deviation. A univariate analysis to identify predictors of survival at the time of oral cancer diagnosis was performed using the Kaplan-Meier method of survival function, using the log-rank test. Statistically significant prognostic variables were first identified in univariate analyses and those found to be significant were tested subsequently with the multivariate Cox proportional hazard model to identify independent predictors of survival.

To accurately compare the staging system, we used four measures to determine precision in staging: hazard consistency, hazard discrimination, explained variation, and likelihood difference [11]. Hazard consistency refers to the homogeneity of patients within the same subgroup, and that they have similar outcomes. This was measured by the likelihood ratio, where if the p-value > 0.5, the model had good hazard consistency. Hazard discrimination refers to a difference in outcomes between patients of different subgroups, who should have demonstrably different outcomes. This was measured by Harrell's C-concordance statistic, where the higher the value, the better was the discrimination between subsequent groups. Explained variation refers to the proportion for which the model can account for variation (dispersion) within the given data set; this is measured by Somer's Delta, with higher values reflecting better explained variation. Likelihood difference assesses the goodness of fit for competing statistical models, and was measured in our study using the difference in log likelihood, with higher values showing better goodness of fit. We compared the statistical models based on all four of these measures and also the curve separation on Kaplan Meier curves.

Statistical analysis was performed using STATA version 14 (StataCorp, TX, USA) and Excel version 2010 (Microsoft, Redmond, WA, USA).

Table 1
Patient and tumour characteristics of cohort.

Age, mean years (range)	55.1 (18–82) years
Male (%)	498 (77)
Tobacco use (%)	314 (49)
Subsite (%)	
Tongue	429 (67)
Floor of mouth	37 (6)
Buccal cavity	173 (26)
Alveolus/retromolar	4 (1)
Pathological TNM Staging by AJCC 8th edition	
pT1	261 (41)
pT2	228 (35)
pT3	59 (9)
pT4a	95 (15)
pN0	372 (58)
pN1	101 (15)
pN2a	10 (2)
pN2b	3 (1)
pN2c	22 (3)
pN3b	135 (21)
Patients having a nodal yield < 18 nodes on dissection	15 (2)
Pathological nodal staging by lymph node ratio	
0	372 (58)
< 0.1	157 (24)
0.1–0.4	78 (12)
> 0.4	36 (6)
Pathological nodal staging by number of positive lymph nodes	
0	372 (58)
1–2	138 (21)
3–4	113 (18)
≥5	20 (3)
Pathological nodal staging by log odds of positive lymph nodes	
−1.69 to −1.29	400 (63)
−1.29 to −0.88	119 (19)
> −0.88	127 (18)
Differentiation (%)	
Well	332 (52)
Moderate	285 (44)
Poor	26 (4.0)
Perineural invasion (%)	222 (35)
Lymphovascular invasion (%)	172 (27)
Extranodal extension (%)	167 (26)
Least tumor margin, median (mm)	7.25
Tumor depth of invasion, median (mm)	12.08
Tumor thickness, median (mm)	12.65
Least tumour margin, median (mm)	6
Close margins (1–5 mm) (%)	39 (6)
Positive margins (< 1 mm) (%)	5 (1)
Adjuvant radiotherapy (%)	171 (27)
Adjuvant chemoradiotherapy (%)	171 (27)
Follow up time, median in years (range)	2.9 (0.5–11)
Recurrence (%)	216 (34)
Time to recurrence, median in years	2.6
Local recurrence (%)	150
Nodal recurrence (%)	68
Distal recurrence (%)	70

Results

Patient and tumour characteristics

The patient and tumour characteristics are shown in Table 1. A total of 643 patients were included in the analysis. Seventy-seven percent of patients were male and 49% of patients had associated tobacco exposure. The sub-sites included were tongue (67%), buccal mucosa (26%), floor of mouth (6%) and alveolus (1%). The pathological T staging by AJCC 8th edition was T1, pT2, pT3 and pT4 in 40.6%, 35.5%, 9.2% and 14.8% respectively. The nodal staging was pN0, pN1, pN2a, pN2b, pN2c and pN3b was 58%, 15%, 2%, 1%, 3% and 21% respectively. Median lymph node yield per neck dissection was 23 (range 12–73), which has been shown to be adequate in previous literature [14,15]. Only 15 patients (2.3%) of patients had a nodal yield of < 18 nodes on dissection. No patients were staged pN3a (node size greater than 3 cm without ENE). Tumour differentiation was well, moderate and poor in 51.6%, 44.3% and 4%. Perineural invasion was seen in 34.5% and lymphovascular invasion in 26.8% of patients. ENE was noted in 26% of node positive patients. Median least margin was 6 mm, with 39 (6%) of patients having close margins (1–5 mm) and 5 (< 1%) having positive margins (< 1 mm). Recurrences were seen in 33.6% of patients, of which 52% were local, 24% were nodal and 24% were distant. Adjuvant radiotherapy was administered to 171 (27%) and chemoradiotherapy to 171 (27%) patients. Median follow-up was 2.9 years (range 0.5–11 years).

Survival analysis (Tables 2 and 3)

Disease free survival

As per AJCC8 patients were categorized into pN0, pN1, pN2a, pN2b, pN2c and pN3b, and had a DFS at five years of 74%, 53%, 50%, 47%, 24% and 0% respectively. Stratification between the stages was seen, with the hazard ratio for recurrence for pN1, pN2a, pN2b, pN2c and pN3b being 1.73, 2.09, 2.48, 4.31 and 5.69 respectively. The worst cohort was stage pN3b (HR 5.69, p = 0.015, 95% CI 1.398–23.205).

Using the PN, there was better discrimination between subsequent stages. The DFS at five years for 0, 1–2, 3–4, ≥5 was 74%, 52%, 27% and 18% respectively. The hazard ratios for recurrence for 1–2, 3–4 and ≥5 were 2.92, 4.68 and 6.07 respectively. The worse cohort was ≥5 nodes (HR 6.07, p = 0.002, 95% CI 3.801–9.712).

While using LNR, the discrimination between subsequent stages was even more pronounced. The DFS at five years for 0, < 0.1, 0.1–0.4 and > 0.4 was 74%, 54%, 37% and 15% respectively. The hazard ratios for < 0.1, 0.1–0.4, > 0.4 were 1.72, 2.72 and 8.24 respectively. The worst prognostic group was > 0.4 (HR 8.24, p < 0.001, 95% CI 4.823–14.083).

For LODDS, there were no patients from our cohort in the lowest risk subcategory (< −1.68). There was good discrimination between the other stages; the DFS at five years for −1.68 to −1.29, −1.29 to −0.88 and > −0.88 was 73%, 62% and 34% respectively. The worst prognostic group was > −0.88 (HR 3.04, p < 0.001, 95%CI 1.103–2.220).

Overall survival

AJCC8 had good discrimination between subsequent stages. The OS at five years for pN0, pN1, pN2a pN2b, pN2c and pN3b were 85%, 73%, 50%, 53%, 20% and 0%. However the hazard ratio did not correlate well with subsequent N-stages. The hazard ratios for pN1, pN2a, pN2b, pN2c and pN3b were 2.71, 5.43, 4.52, 6.80 and 9.69 respectively. pN3b was the worst prognostic cohort (HR 9.69, p < 0.001, 95% CI 1.398–23.205).

PN had better discrimination between subsequent stages than AJCC8. The OS for 0, 1–2, 3–4, ≥5 was 85%, 70%, 27% and 18% respectively. The hazard ratios for recurrence for 1–2, 3–4 and ≥5 were 2.73, 7.27 and 14.30 respectively. The worse cohort was ≥5 nodes (HR 14.30, p < 0.001, 95% CI 8.099–25.259).

For LNR the discrimination between subsequent stages was even more pronounced. The DFS for 0, < 0.1, 0.1–0.4 and > 0.4 was 85%, 73%, 52% and 14% respectively. The hazard ratios for < 0.1, 0.1–0.4, > 0.4 were 1.72, 2.72 and 23.07 respectively. The worst prognostic group was > 0.4 (HR 23.07, p < 0.001, 95% CI

Table 2
Predictors of recurrence in different nodal staging systems on multivariate analysis by Cox proportional hazards regression model.

Stage	5 year disease free survival	Hazard ratio	p-value	95% CI		Likelihood ratio	Harrell's C-concordance index	Somer's Delta	Difference in log likelihood
AJCC 8th edition						0.2972	0.7103	0.4206	−1202.988
pN0	74%	Referent							
pN1	53%	1.73	0.006	1.175		2.571			
pN2a	50%	2.09	0.148	0.769		5.691			
pN2b	47%	2.48	< 0.001	1.814		3.401			
pN2c	24%	4.31	< 0.001	2.502		7.447			
pN3b	0%	5.69	0.015	1.398		23.205			
Number of positive nodes (PN)						**0.4516**	**0.7156**	**0.4312**	**−120.5.522**
0	74%	Referent							
1–2	52%	1.64	0.003	1.184		2.277			
3–4	27%	3.74	< 0.001	2.565		5.464			
≥5	18%	6.07	0.002	3.801		9.712			
Lymph node ratio (LNR)						0.4147	0.7145	0.4290	−1202.675
0	74%	Referent							
< 0.1	54%	1.72	< 0.001	1.232	2.412				
0.1–0.4	37%	2.72	< 0.001	1.943	3.826				
> 0.4	15%	8.24	< 0.001	4.823	14.083				
Log odds of positive lymph nodes (LODDS)						0.1988	0.7079	0.4776	−1205.150
−1.69 to −1.29	73%	Referent							
−1.29 to −0.88	62%	1.56	< 0.0001	1.24	2.220				
> −0.88	34%	3.04	< 0.001	0.86	4.143				

Table 3
Predictors of survival in different nodal staging systems on multivariate analysis by Cox proportional hazards regression model.

Stage	5 year disease free survival	Hazard ratio	p-value	95% CI		Likelihood ratio	Harrell's C-concordance index	Somer's Delta	Difference in log likelihood
AJCC 8th edition						0.2244	0.7503	0.5006	−648.861
pN0	85%	Referent							
pN1	73%	2.71	< 0.001	1.572	4.694				
pN2a	50%	5.43	0.001	1.932	15.313				
pN2b	53%	4.52	< 0.001	2.906	7.033				
pN2c	20%	6.80	< 0.001	5.029	18.692				
pN3b	0%	9.69	0.059	0.927	49.847				
Number of positive nodes (PN)						**0.5349**	**0.7600**	**0.5200**	−645.177
0	85%	Referent							
1–2	70%	2.73	< 0.001	1.718	4.338				
3–4	27%	7.27	< 0.001	4.016	11.207				
≥5	18%	14.30	< 0.001	8.099	25.259				
Lymph node ratio (LNR)						0.5314	0.7552	0.5104	**−650.6454**
0	85%	Referent							
< 0.1	73%	2.92	< 0.001	1.825	4.671				
0.1–0.4	52%	4.68	< 0.001	2.904	7.551				
> 0.4	14%	23.07	< 0.001	12.340	43.139				
Log odds of positive lymph nodes (LODDS)						0.2954	0.7388	0.4776	−643.786
−1.69 to −1.29	80%	Referent							
−1.29 to −0.88	73%	2.28	0.001	1.412	3.707				
> −0.88	48%	5.36	< 0.001	3.531	8.153				

12.340–43.139).

For LODDS, there was good discrimination between the other stages; the DFS at five years for −1.68 to −1.29, −1.29 to −0.88 and > −0.88 was 80%, 73% and 48% respectively. The worst prognostic group was > −0.88 (HR 5.36, p < 0.001, 95%CI 3.531–8.153).

Comparing the performance of the staging systems

Prediction of recurrence

For DFS, visual inspection of the Kaplan Meier curves revealed that PN and LNR provided the best curve separation (figure 1). When comparing the hazard consistency, both PN and LNR had the highest likelihood ratios (0.4516 and 0.4147), but neither were greater than 0.5. When comparing hazard discrimination, PN and LNR had the highest C-statistic values (0.7156 and 0.7145 respectively). In term of explained variation, again, PN and LNR had the higher Somer's Delta (0.4312 and 0.4290 respectively). The likelihood difference was similar in all staging systems.

Prediction of survival

For OS, visual inspection of the Kaplan Meier curves revealed that PN provided the best curve separation (Fig. 2). When comparing the hazard consistency, both LNR and PN had likelihood ratios (p > 0.5) with comparable results. When comparing hazard discrimination, PN and LNR had the highest C-statistic values (0.7600 and 0.7552 respectively). In term of explained variation, again, PN and LNR had higher Somer's Delta (0.5200 and 0.5104 respectively). The likelihood difference was similar in all staging systems. When considering prediction of both recurrence and survival, PN and LNR were the best staging systems in terms of hazard consistency and discrimination, explained variation and likelihood difference.

Discussion

The recent AJCC 8th edition recommended changes in the nodal staging of head and neck cancers [3]. These were made based on the analysis of a pooled database of patients from two institutions; Memorial Sloan Kettering Cancer Centre, New York and Princess Margaret Hospital, Toronto, which was then validated on the National Cancer Database [3,8]. Although a significant improvement in precision in staging was observed, some of the limitations of the previous AJCC nodal staging were not addressed. These include the doubtful value of bilateral nodal disease, poor discrimination between N2 sub-stages and inability to correct for inadequacy of neck dissection and nodal yield.

External validations of the AJCC 8th edition have been published. Matos et al [12] compared the AJCC 7th edition and 8th edition for oral cancer in a cohort of 298 patients and found that patients upstaged due to the presence of ENE had a significantly worse disease free and overall survival than those who did not; however, the survival curves for pN2a, pN2b and pN2c overlapped. The discrimination of sub-stages within pN2 was insufficient to predict recurrence or survival. Garcia et al [13] compared the pathological lymph node staging for multiple sub-sites of head and neck SCC, of which 270 patients had OSCC. They too found that upstaging by ENE improved discrimination between stages pN1, pN2 and pN3 for cause specific survival; however, outcomes in sub-stages (N2a, N2b, N2c, N3a and N3b) were not specified.

Our data suggests that these limitations persist in the 8th edition of AJCC. With respect to DFS, there was good stratification with consecutive stages showing higher hazard ratios for recurrence, but there were negligible differences in stages pN1-pN2b for DFS or stages pN2a-pN2c for OS. The hazard ratios for pN2a and pN2b were comparable, with no discernable difference in clinical outcomes. Overall, there was insufficient prognostication between subsequent nodal stages in this system. Discrimination between sub-stages of N2 was poor, in spite of upstaging those with ENE in lymph nodes larger than 3 cm in size to pN3b.

Interestingly, in our cohort, the role of bilateral nodal disease (stage pN2c) was found to have a significant impact on DFS and OS (hazard ratios 4.31 and 6.80 respectively), which was not seen with the AJCC 7th edition [4,7]; these studies showed that pN2c did not have a higher propensity for recurrence or survival than pN2b disease. This finding in our cohort may be a result of incorporation of ENE into the AJCC 8th edition. Previously the distribution of ENE between the sub-stages of N2 may have varied, resulting in heterogeneity of outcomes. By incorporating ENE into nodal staging, AJCC 8th edition has likely improved prognostication, especially in the high-risk group.

Inadequacy of neck dissection results in incomplete treatment and a poor outcome. Ebrahimi et al [14] demonstrated that patients of OSCC

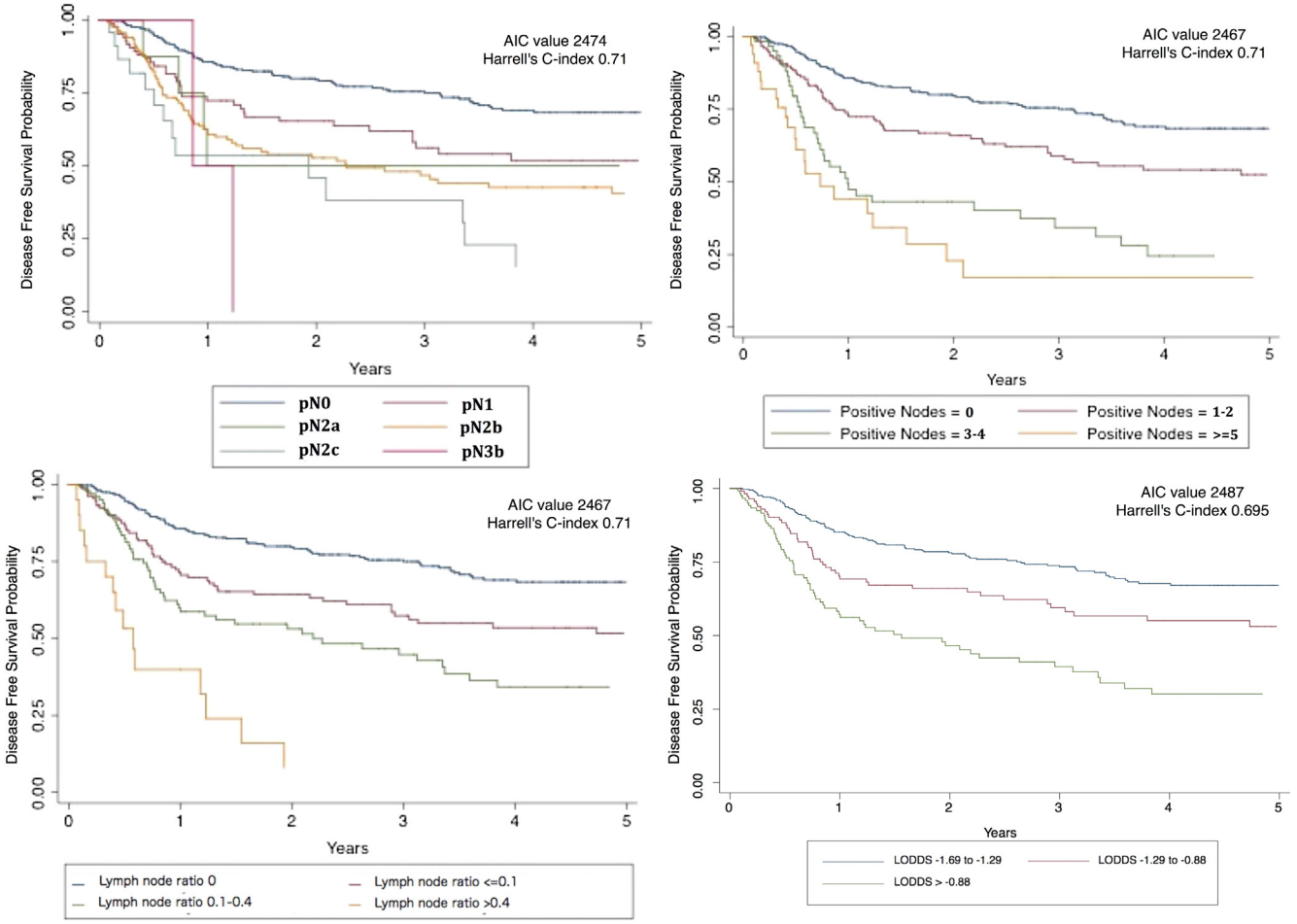

Fig. 1. Disease free survival in OSCC as determined by four lymph nodal staging systems.

with eighteen nodes or more on neck dissection had an improved survival, suggesting that this was an adequate nodal yield. LNR takes into account the total number of lymph nodes excised. LNR has been shown by multiple authors [6,15–18] to be a consistent predictor of survival in head and neck cancers after first being demonstrated as a prognostic tool in other tumours, such as bladder, oesophageal and cervical cancers. It measures tumour burden correcting for nodal yield, which is likely to vary with extent of neck dissection. This may be one of the reasons for the excellent performance of lymph node ratio in our cohort, as evident both on multivariate analysis and clinical outcomes.

PN was recently shown by Roberts et al [7] to be superior to LNR in a cohort of over twelve thousand patients of oral and oropharyngeal SCC from the SEER database. This is reflected in the incorporation of PN into the pathological staging of HPV positive oropharyngeal cancers in the AJCC 8th edition staging [3]. PN has also been shown in a recent publication by Rajappa et al [19] to outperform AJCC 8th edition in prediction of OS and DFS, albeit with different cut-offs (0 nodes, 1 node, 2 nodes and > 2 nodes). In our data, PN, like LNR, outperformed AJCC 8th edition; it was a better predictor of survival and recurrence, with better inter-stage discrimination and separation of the Kaplan-Meier curves. The hazard ratio on multivariate analysis was further evidence of this. The likely explanation for this is that the number of positive nodes is a better reflection of disease burden than node size especially in the absence of ENE.

PN and LNR outperformed AJCC8 and LODDS on prediction of OS and DFS. It is our belief that PN may be a more reliable staging system. The reason why LNR may be less accurate than PN is fairly straightforward; in his paper on nodal yield, Ebrahimi [11] showed that although patients with more than eighteen nodes in the neck dissection specimen had better survival, the relation between nodal yield and survival was non-linear. When nodal yield increased beyond 32 nodes, survival actually reduced; the authors attributed this to the likelihood that those with higher nodal yields had more extensive neck dissection due to clinical suspicion of aggressive primary tumours, which could cause an artificial reduction in lymph node ratio in a subset of patients. This is an important drawback of LNR that is almost impossible to adjust for when used as a staging system for nodal disease. This also makes it less suitable for adoption as a staging system – the extent of neck dissection varies significantly between primary tumour and institutional policy. Early node-negative oral cancer is often treated with a supraomohyoid neck dissection and node-positive oral cancer is treated with selective neck dissection (levels I–IV) or modified radical neck dissection (levels I–V), all of which are likely to have different nodal yields.

LODDS is calculated by determining the logarithm of the lymph node ratio, and has also been showed to be a good predictor of survival in OSCC [9,10,20]. A study of nearly 4000 OSCC patients by Safi [20] demonstrated that the log odds of positive lymph nodes performed better over AJCC8, LNR and PN. LODDS performed well on our cohort as well, however it was inferior to PN. Like LNR, it is also potentially affected by high nodal yield in aggressive neck dissection. Some major differences between our study and Safi's are to be noted; firstly, we did not have any patients in the low risk group ≤ -1.68 and we used different cut-offs for lymph node ratio (they used cut-offs of 0.2 and 0.4 for LNR, while we used 0.1 and 0.4, which we believe results in better stage discrimination). Both these are likely to have impacted our analysis.

When compared with AJCC8 and LODDS, our data suggested that

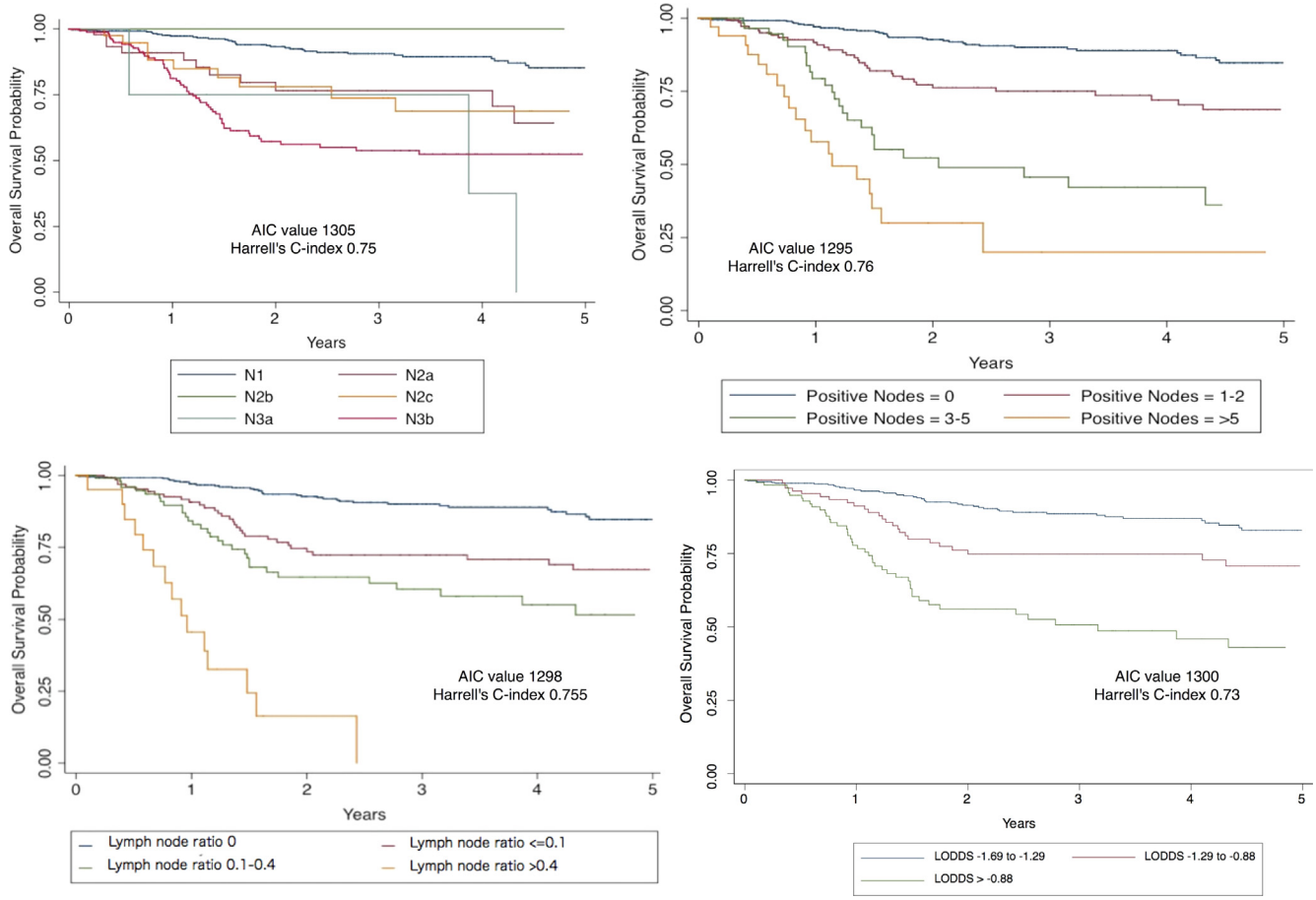

Fig. 2. Overall survival in OSCC as determined by four lymph nodal staging systems.

PN and LNR were better predictors of recurrence and survival in terms of hazard consistency and discrimination, explained variation and likelihood difference. It is relevant, however, to note that amongst all these staging systems, only AJCC8 can be determined both clinically and pathologically. Whether OSCC would benefit from a separate pathological staging in the form of number of positive lymph nodes or lymph node ratio, like HPV-positive oropharyngeal cancer, is a relevant question. Surgically treated HPV-negative head and neck cancers remain the only cancers that have a size-based pathological nodal staging system [3]; other cancers like non-melanoma skin cancers, malignant melanoma, gastrointestinal cancers and breast cancer all rely on number of positive lymph nodes to prognosticate and stage patients. It is our opinion that adopting this as the pathological staging for oral cancer would significantly improve the precision of staging while simplifying it considerably.

In addition to having good prognostic grouping, PN is also arguably the simplest staging system available. As it is a direct reflection of tumour burden, it remains unaffected by potential confounders like laterality of nodal disease and nodal yield. It may also be valuable in the setting of central oral cavity tumours, where contralateral nodal disease may be artificially upstaged. It is relevant, however, that only 15 patients in our cohort (2.3%) had less than 18 nodes on their neck dissection; hence we are unable to comment on whether number of positive lymph nodes is still an accurate staging system in the incompletely dissected neck. Our data suggests it is the most suitable lymph node staging system currently available for oral cancer in the adequately dissected neck. As oral cancer is a disease predominantly treated by surgery, a more accurate pathological staging system would allow better prognostication and identifying high-risk groups for potential treatment intensification.

Conclusion

PN and LNR were the most accurate lymph node staging systems in our cohort of OSCC, with comparable performance. PN is an easier and more reliable parameter, especially in heterogenous patient cohorts. Incorporation of this parameter into future staging systems would help better prognosticate patients and address the pitfalls of the AJCC staging system.

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