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Outcomes of Curative (Chemo)Radiotherapy for Patients With Non-p16 Positive Head and Neck Squamous Cell Carcinoma Who Are Borderline for Curative Treatment

Outcome of borderline curable HNSCC

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1 ABSTRACT

2
3 **Background:** Appropriate selection of head and neck squamous cell cancer
4 (HNSCC) patients for curative treatment is difficult, and it's a very understudied issue.
5 The aim of this study was to review the outcomes of curative intent treatment in non-
6 p16 positive HNSCC patients assessed as having borderline curability.
7

8 **Methods:** A single institution retrospective review of the clinical outcomes of non-
9 p16 positive HNSCC patients with borderline curability. Predefined criteria for
10 borderline curability were: 1) T4 and/or N3 disease; or 2) ECOG status ≥ 2 ; or 3) age
11 ≥ 75 years.
12

13 **Results:** 114 patients were identified. 56 had N3/T4, 32 were $> \text{ECOG } 2$ and 57
14 were > 75 years. 29 had 2 or more borderline curability criteria. Progression free
15 survival rate (PFS) at 1 and 2 years was 72% (95% confidence interval [CI], 63-79)
16 and 53% (95% CI, 43-62), respectively. Overall survival (OS) at 1 and 2 years was
17 76% (95% CI, 67-83) and 61% (95% CI, 51-69), respectively. On multivariable
18 analysis, the only independent prognostic factor for OS was the adult comorbidity
19 evaluation-27 (ACE-27) grade (HR 1.4; 95% CI, 1.1-1.8; $p=0.018$).
20

21 **Conclusions:** Patients with borderline curability criteria treated with curative intent
22 achieved good PFS and OS. ACE-27 was an important prognostic factor in this
23 population.
24

25 Key words:

26 head and neck cancer, adult comorbidity evaluation-27 (ACE-27), squamous cell
27 carcinoma, borderline curability, elderly
28

29 Author Contribution:

30 Daniel Xing: data collection, data analysis, and writing – original draft; Albert Tiong:
31 conceptualization, writing – review and editing; Mathias Bressel: data analysis,
32 writing – review and editing; Danny Rischin: writing – review and editing; Philip Tran
33 –data collection, review and editing; June Corry: Conceptualization, writing – review
34 and editing

Introduction

The responsibility for appropriate selection of head and neck squamous cell cancer (HNSCC) patients for curative intent non-surgical treatment, rather than palliative treatment, can be one of the most difficult tasks for treating oncologists. On the one hand, we don't want to undertreat patients, but neither do we want to subject them to curative intent treatment regimens with their inherent severe acute toxicities without a reasonable expectation of cure, or at least a "reasonable" duration of progression free survival (PFS). There is in fact no data on what HNSCC patients think is "reasonable" as to the minimal time period free of disease symptoms and treatment toxicities that would justify significant acute treatment-related toxicity¹. Similarly, there is no universal agreement as to what constitutes incurable or borderline curable disease. Elderly patients and patients with poor performance status are underrepresented in clinical trials²⁻⁵. Furthermore, there can be clinician non-selection of patients with large volume disease who are felt to be of borderline curability for enrolment into clinical trials. Hence translating the results of such trials into everyday clinical practice may be inappropriately optimistic. There is no data in the literature to support an evidence-based recommendation regarding appropriate selection of HNSCC patients for curative intent non-surgical treatment.

As there is currently no definition of what constitutes "borderline curability" or a "reasonable PFS", we defined these terms *a priori*. Borderline curability was defined as patients with T4 or N3 disease, ECOG ≥ 2 , or age ≥ 75 years. Human papilloma virus (HPV)-positive oropharyngeal squamous cell carcinoma represents a distinct subgroup of head and neck cancers associated with good clinical outcome even in those with locally advanced disease (i.e. T4 or N3 disease). Therefore, for this study we excluded patients with p-16 positive oropharyngeal cancer. In addition, the authors formed a consensus that at least a 12-month progression free survival was required to justify the 7 weeks of curative intent treatment and subsequent approximately 6 weeks for resolution of acute treatment toxicities, an overall period of about 3 months.

The aim of this study was to review the clinical outcomes of all non-p16 positive HNSCC patients of borderline curability treated with curative intent (chemo)radiotherapy.

Methods

This was a retrospective review of a prospective head and neck cancer database and electronic patient records. Patients were selected from the database if they were treated at Peter MacCallum Cancer Centre from 1st January 2004 to 31st December 2011 with a pathological diagnosis of primary mucosal squamous cell carcinoma of oral cavity, oropharynx, larynx, and hypopharynx. Patients with borderline curability were defined as those with one or more of the following criteria: 1) T4 and/or N3 disease, 2) ECOG status ≥ 2 , 3) age ≥ 75 -years. Patients' ECOG and ACE-27 were derived from their electronic medical records. Curative intent treatment could be with either radiotherapy or chemoradiotherapy, or induction chemotherapy followed by (chemo)radiotherapy. Curative intent treatment was defined as a biological equivalent dose of 66Gy in 2Gy fractions, or higher. Exclusion criteria included oropharynx p16 positive patients, patients with nasopharyngeal and paranasal sinus carcinoma, histology other than squamous cell carcinoma, previous high dose head and neck radiotherapy, or distant metastatic disease.

Study Outcomes

The primary end points were progression free survival (PFS) and overall survival (OS). PFS was measured from the date of treatment commencement until the date of first progression or date of death from any cause, whichever occurred first. Patients who were not known to have progressed or died were censored at the date of last follow-up. OS was measured from the date of treatment commencement until the date of death from any cause. Patients who were not known to have died were censored at the date of last follow-up. Pattern of first failure - measured from the date of treatment commencement to the date of first failure (local failure, nodal

failure or distant failure). A secondary endpoint was assessment of the utility of a patient selection algorithm retrospectively applied to this patient cohort (Figure 1).

Statistical Analysis

Baseline characteristics were summarised using descriptive statistics including counts and frequencies for categorical variables and mean, standard deviation (SD), median and range for continuous variables. Kaplan-Meier methods were used to display the OS and PFS curves. Cumulative incidence curves of first failure were provided assuming competing risks. Cox proportional hazard models were used to assess the impact of candidate prognostic factors on overall survival. The assumption of i) proportional hazards, and ii) linearity (for continuous variables) were verified. The presence of influential observations was also assessed. Treatment completion rate and patient treatment recommendation according to the retrospectively applied algorithm was described as counts and percentages. All statistical analyses were performed in R 3.2.3⁶.

Results

Patient Characteristics

There were 114 patients who fulfilled the eligibility criteria. The frequency of each of the criteria for borderline curability are shown in the Figure 2. Patient's clinical characteristics are summarized in Table 1. There were 14 patients with oral cavity tumours that were treated with definitive (chemo)radiation: Nine of the 14 had T4 oral tongue tumours that would have necessitated a total glossectomy, so the multidisciplinary meeting (MDM) recommendation was for chemoradiotherapy⁷. Of the remaining 5 patients: 1 with a T4N2a retromolar trigone SCC, 1 with a T2N0 SCC of the buccal mucosa on the inside of the upper lip, 1 with a previously resected oral tongue cancer who had an inoperable 8 cm nodal recurrence, 1 with bilateral nodal recurrence from a previously excised hard palate SCC, and 1 with a large

T2N2b oral tongue SCC, were also recommended to have (chemo)radiotherapy by the MDM.

Nearly all the patients (99% [113/114]) were treated with the equivalent of 66Gy or 70Gy in 2Gy fractions, and 59.6% [68/114] had concurrent chemotherapy, of which the commonest regimen was cisplatin 100mg/m² in weeks 1, 4 and 7 (Table 1). There were 12 patients treated with induction chemotherapy, 11 of whom were then deemed suitable for curative intent chemoradiotherapy. One patient underwent palliative RT (QUAD SHOT) ⁸ post induction chemotherapy due to poor response.

The overall treatment completion rate was 93.9% (n=107/114). Seven patients did not complete the radiotherapy due to death during treatment (n=4), non-compliance (n=2), and poor response (n=1).

Patient outcomes

The median follow-up was 5.3 years (range 2 weeks to 9.4 years). The 1 and 2-year PFS rates were 72% (95% CI, 63-79) and 53% (95% CI, 43-62), respectively. The 1 and 2-year OS rates were 76% (95% CI, 67-83) and 61% (95% CI, 51-69), respectively (Figure 3). The cumulative incidence of local only failure, nodal only failure and distant only failure at 2 years were 8%, 4% and 7% respectively, and 5-year were 9%, 4%, and 9%, respectively (supplementary figure). Of the 72 deaths, 29 (40%) died free from cancer, 19 (26%) died with persistent disease, 14 (19%) died with recurrent disease and 10 (14%) died with second malignancy.

Prognostic factors for overall survival

The assessment of prognostic factors for overall survival is shown in Table 2. Patients with higher ACE-27 grade (HR 1.3 per grade increase; 95% CI, 1.0-1.6; p=0.018) had worse overall survival (Figure 4). Using ACE-27 grade dichotomized as grade 0-1 vs. 2-3, the adjusted HR for patients with ACE-27 grade 2-3 in relation to ACE-27 grade 0-1 was 2.2 (95% CI, 1.3-3.7; p=0.004). The details of patient and tumour characteristics by ACE-27 are shown in Table 3.

Patient selection algorithm for curative intent treatment in non-p16 positive HNSCC and treatment outcome

We previously designed a patient selection algorithm for decision making regarding radical or palliative treatment (Figure 1)⁹. We applied this algorithm retrospectively to see if it was feasible to document our clinical experience into a decision-making flow chart that reflected our management approach in selecting non-p16 positive oropharyngeal patients with borderline curability for curative intent treatment. Applying this tool retrospectively, 23 (20%) patients shouldn't have been selected to receive curative intent treatment according to the selection algorithm. The adverse factors of these patients were: 1) ECOG 3 (n=7); and 2) more than two adverse factors (n=16, supplementary Table 1 and 2). Interestingly these 23 patients had a similar treatment completion rate (87% [20/23] vs. 96% [87/91], p=0.29) but they had a lower progression free survival (2 years PFS of 28% [95% CI, 11 - 47] vs 59% [95% CI, 48 - 69]; HR 2.2 [95% CI, 1.3 – 3.7]; p = 0.003) and overall survival (2 years OS of 32% [95% CI, 14 - 51] vs 68% [95% CI, 57 - 77]; HR 2.51 [95% CI, 1.5 – 4.3]; p<0.001), compared to the curative intent patients as per the algorithm.

Discussion

There is very little research in the domain of appropriate selection of HNSCC patients for curative intent treatment. This is the first study to show that curative intent (chemo) radiotherapy in patients assessed as borderline for curative treatment can result in good PFS and OS. Our *a priori* consensus was that patients needed to obtain at least 12 months PFS to justify the duration and toxicity of curative intent (chemo)radiotherapy. This was achieved in the vast majority [72% (95% CI, 63-79)] of patients, and there was a 2-year PFS of 53% (95% CI, 43-62). The toxicities of curative intent (chemo)radiotherapy are severe and so this data was clinically reassuring in that it supported our *a priori* consensus.

We think the clinical algorithm proposed could be a useful tool to aid appropriate selection of patients for curative intent or palliative treatment in non-p16 positive HNSCC. It was created in an attempt to distil our clinical experience into a decision-making flow chart that reflected our management approach to patients with borderline performance status and/or large volume disease. The algorithm incorporates information from previous studies showing that performance status,

TNM stage and age are prognostic factors for patient with head and neck cancer ¹⁸.
¹⁹. Given that we showed retrospectively the algorithm encompassed the
management plan of 80% of the patients, and that patients treated in accordance
with the algorithm had a better PFS and OS, we think it is a clinically useful tool.
Following the results of this study showing that ACE-27 is the only prognostic factor
for overall survival (Table 2), we subsequently modified our original algorithm to
incorporate ACE-27 (Figure 5). Clearly such a tool needs to be validated in
prospective studies using appropriate methodology, but it would seem that it could
have utility in this difficult area of appropriate selection of HNSCC patients for
curative intent treatment.

A large proportion (53%) of this patient cohort had significant medical co-morbidities
with an ACE-27 Grade of 2-3, and 28% were ECOG 2 or 3. The relationship between
ACE-27 and ECOG status is shown in supplementary Table 3. Performance status
(e.g. ECOG) has been well documented as a significant prognostic factor for OS in
many diseases, including HNSCC ¹⁰. Whilst performance status is frequently
documented clinically, the clinical use of a comorbidity index is perhaps less routine.
It has been reported that comorbidity is present in 30-55% patient with HNSCC ¹¹.
The ACE-27, also known as the modified Kaplan Feinstein comorbidity index (KFI),
has been shown to be a reliable and easy to use tool to code and quantify the
presence of comorbidity in HNSCC patient compared with cumulative illness rating
scale (CIRS), the Charlson comorbidity index (CCI) and the index of coexistent
disease (ICED) ^{12, 13}. It is worth noting that the variability of ACE-27 score is small,
thus applying ACE-27 alone in differentiating patients is of limited value. Therefore,
we incorporated the ACE-27 in the decision making algorithm (Figure 5).

The other predominant group in our patient cohort was the elderly. There is no true
definition of “elderly” in HNSCC. Publications on the “elderly” include patients as
young as 65 years ¹⁴, but the most frequently used cut-off is for those patients 70-75
years or older. In our cohort, there were 57 (50%) patients 75 years or more.
Appropriate management of elderly patients is important as our population ages.
Currently it is anticipated that in the next 30 years the number of people over 85
years will more than double ¹⁵. The MACH-NC meta-analysis ¹⁵ suggested that the
survival advantage of concurrent chemoradiotherapy was less significant for patients

more than 75 years. In a large retrospective study [16] of HNSCC patients who were selected for definitive radiotherapy, 238 elderly patients (75 years or older) did not show difference in treatment interruption, completion rates, or treatment-related deaths compared with 1249 younger patients. It has also been reported that increased age did not affect overall survival or loco-regional control in an analysis of 1589 patients from five EORTC prospective radiotherapy trials, but the occurrence of significant mucosal reactions is associated with increasing age ¹⁷. However, only 30 patients (1.9%) in that analysis were older than 75 years. In our study, we did not find that age was an independent predictor of overall survival on multivariable analysis. It seems patient's ACE27 grade are more relevant than their age per se.

A major weakness in this study is that our results are based only on PFS and OS, with no information on patient reported outcomes (PRO) or quality of life (QOL) during and after treatment. There is in fact no good patient derived data in HNSCC that can guide the decision about clinical appropriateness of curative therapy. There is currently no data about patient derived utilities for the various potential patient health states both during and after treatment. Neither do we know what payoff HNSCC patients would accept for the various treatment options. This is an important area for future research in this patient population.

Whilst we limited this study to patients treated non-surgically, we think the clinical dilemma of appropriate patient selection is as, if not more, valid for HNSCC patients with disease subsites usually treated surgically. We plan to complete a similar study in a surgical cohort of patients of borderline curability.

Conclusion

This group of patients fulfilling our predetermined borderline curability criteria and treated with curative intent had greater than 12 months PFS in the vast majority of patients. Hence we were reassured that we weren't inappropriately "over treating" these patients. Patient's ACE-27 was an important predictor for overall survival in this borderline curable population. We have retrospectively developed a patient selection tool that accounted for 80% of the patients in this study and warrants prospective validation.

References

1. Solem CT, Kwon Y, Shah RM, Aly A, Botteman MF. Systematic review and benchmarking of Quality-Adjusted Time Without Symptoms or Toxicity (Q-TWiST) in oncology. *Expert Rev Pharmacoecon Outcomes Res.* 2018;1-9.
2. Denis F, Garaud P, Bardet E, et al. Final results of the 94-01 French Head and Neck Oncology and Radiotherapy Group randomized trial comparing radiotherapy alone with concomitant radiochemotherapy in advanced-stage oropharynx carcinoma. *J Clin Oncol.* 2004;22:69-76.
3. Ang KK, Harris J, Wheeler R, et al. Human papillomavirus and survival of patients with oropharyngeal cancer. *N Engl J Med.* 2010;363:24-35.
4. Bonner JA, Harari PM, Giralt J, et al. Radiotherapy plus cetuximab for squamous-cell carcinoma of the head and neck. *N Engl J Med.* 2006;354:567-578.
5. Forastiere AA, Goepfert H, Maor M, et al. Concurrent chemotherapy and radiotherapy for organ preservation in advanced laryngeal cancer. *N Engl J Med.* 2003;349:2091-2098.
6. Team RC. A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. 2015.
7. McDowell L, Collins M, Kleid S, Rischin D, Corry J. T4 squamous cell carcinoma of the oral tongue without mandibular involvement: surgery or chemoradiotherapy? *Oral Surg Oral Med Oral Pathol Oral Radiol.* 2014;117:163-169.
8. Corry J, Peters LJ, Costa ID, et al. The 'QUAD SHOT'--a phase II study of palliative radiotherapy for incurable head and neck cancer. *Radiother Oncol.* 2005;77:137-142.
9. Tjong A, Corry J. Head and neck. In: C J, ST L, eds. *Handbook of Palliative Radiation Therapy.* New York, NY, United States: Demos Medical Publishing; 2016:99-117.
10. Yates JW, Chalmer B, McKegney FP. Evaluation of patients with advanced cancer using the Karnofsky performance status. *Cancer.* 1980;45:2220-2224.
11. Piccirillo JF, Tierney RM, Costas I, Grove L, Spitznagel EL, Jr. Prognostic importance of comorbidity in a hospital-based cancer registry. *JAMA : the journal of the American Medical Association.* 2004;291:2441-2447.

- 303 12. Hall SF, Rochon PA, Streiner DL, Paszat LF, Groome PA, Rohland SL.
304 Measuring comorbidity in patients with head and neck cancer. *Laryngoscope*.
305 2002;112:1988-1996.
- 306 13. Datema FR, Ferrier MB, van der Schroeff MP, Baatenburg de Jong RJ.
307 Impact of comorbidity on short-term mortality and overall survival of head and
308 neck cancer patients. *Head Neck*. 2010;32:728-736.
- 309 14. The National Academies of Sciences E, and Medicine. Delivering high-quality
310 cancer care: charting a new course for a system in crisis. 2013.
- 311 15. Australian Government. 2015 Intergenerational Report: Australian in 2055.
312 2015
- 313 16. Pignon JP, le Maitre A, Maillard E, Bourhis J, Group M-NC. Meta-analysis of
314 chemotherapy in head and neck cancer (MACH-NC): an update of 93
315 randomised trials and 17,346 patients. *Radiother Oncol*. 2009; 92: 4-14.
- 316 17. Huang SH, O'Sullivan B, Waldron J, et al. Patterns of care in elderly head-
317 and-neck cancer radiation oncology patients: a single-center cohort study. *Int*
318 *J Radiat Oncol Biol Phys*. 2011; 79:46-51.
- 319 18. Egelmeier AG, Velazquez ER, de Jong JM, et al. Development and validation of
320 nomogram for prediction of survival and local control in laryngeal carcinoma patients
321 treated with radiotherapy alone: a cohort study based on 994 patients. *Radiother*
322 *Oncol*. 2011; 100: 108-115.
- 323
- 324 19. Fakhry C, Zhang Q, Nguyen-Tan PF, et al. Development and validation of
325 nomogram predictive of overall and progression-free survival in patients with
326 oropharyngeal cancer. *J Clin Oncol*. 2017; 35: 4057-4065.

Figure Legends

Figure 1: Algorithm for selecting patients with non-p16 +ve head and neck squamous cell carcinoma (HNSCC) for curative treatment.

Figure 2. Venn diagram of eligibility criteria for patients with borderline curability.

Figure 3. Progression free survival (A) and overall survival (B) curve. Dashed line represent 95% confidence intervals.

Figure 4. Overall survival by Adult Co-morbidity Evaluation 27 (ACE-27)

Figure 5: Revised algorithm for selecting patients with non-p16 +ve head and neck squamous cell carcinoma (HNSCC) for curative treatment.

Supplementary figure: Cumulative incidence of first failure

Tables

Table 1. Patient and tumor characteristics

Table 2: Prognostic factors for overall survival

Table 3. Patient and tumour characteristics by ACE-27

Supplementary table 1: Clinical details of patient with ECOG 3 who should have been considered for palliative treatment

Supplementary table 2: Clinical details of patient with ECOG ≤ 2 who should have been considered for palliative treatment or induction chemotherapy but received radical treatment

Supplementary table 3: Patient characteristic in ACE-27 by ECOG

Table 1. Patient and tumor characteristics

Variable	Level	Result (n=114)
Gender	Female	20 (17.5%)
	Male	94 (82.5%)
Age	Mean (SD)	71 (13)
	Median [range]	75 [21 - 96]
Criteria for borderline treatment	Age $\geq$ 75	33 (28.9%)
	ECOG $\geq$ 2	7 (6.1%)
	ECOG $\geq$ 2 & Age $\geq$ 75	18 (15.8%)
	ECOG $\geq$ 2 & T4 or N3	5 (4.4%)
	ECOG $\geq$ 2 & T4 or N3 & Age $\geq$ 75	2 (1.8%)
	T4 or N3	45 (39.5%)
	T4 or N3 & Age $\geq$ 75	4 (3.5%)
Subsite	Glottis	44 (38.6%)
	Hypopharynx	14 (12.3%)
	Oral cavity	14 (12.3%)
	Oropharynx (p16 negative)	20 (17.5%)
	Supraglottis	22 (19.3%)
ECOG	0	29 (25.4%)
	1	53 (46.5%)
	2	25 (21.9%)
	3	7 (6.1%)
Smoking	Current smoker	47 (42.7%)
	Ex-smoker	56 (50.9%)
	Non smoker	7 (6.4%)
	Missing	4
T stage	1	20 (17.5%)
	2	24 (21.1%)
	3	23 (20.2%)
	4	47 (41.2%)
N stage	0	58 (50.9%)
	1	10 (8.8%)
	2A	2 (1.8%)
	2B	11 (9.6%)
	2C	18 (15.8%)
	3	15 (13.2%)
Baseline Hb (g/dL)	Mean (SD)	135.2 (16.1)
	Median [range]	139 [101 - 174]

Variable	Level	Result (n=114)
ACE 27	Interquartile range	123.5 - 146.0
	Missing	19
	0	16 (14.0%)
	1	38 (33.3%)
	2	37 (32.5%)
Living condition	3	23 (20.2%)
	Supported	103 (91.2%)
	Unsupported	10 (8.8%)
	Missing	1
Weight loss at baseline	No weight loss	64 (58.7%)
	<10%	27 (24.8%)
	>10%	18 (16.5%)
	Missing	5
Concurrent chemotherapy	No	46 (40.4%)
	Yes	68 (59.6%)
	Cisplatin 100mg/m ² weeks 1,4 and 7	28
	Weekly cisplatin 40mg/m ²	1
	Carboplatin/5FU	25
	Carboplatin	1
	Cetuximab	8
	Cetuximab/Carboplatin	4
	Cisplatin/Tirapazamine	1
Induction of chemotherapy	No	102 (89.5%)
	Yes	12 (10.5%)
EQD2 (Gy)	15.75 (quadshot)	1 (0.9%)
	66 (66Gy/33f)	2 (1.8%)
	66.21 (59.4Gy/33f)	15 (13.2%)
	67.31 (63Gy/28f)	17 (14.9%)
	70 (70Gy/35f)	62 (54.4%)
	70.2 (66Gy/35f)	17 (14.9%)

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Table 2: Prognostic factors for overall survival

Variable	Level	N	Events	Univariable		Multivariable (full model)		Multivariable (simplified model)	
				HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value
Subsite	Oropharynx	20	14	ref	0.569	ref	0.391		
	Oral cavity	14	8	0.5 (0.2-1.3)		0.7 (0.3-2.0)			
	Hypopharynx	14	9	0.7 (0.3-1.7)		0.4 (0.2-1.2)			
	Larynx	66	41	0.8 (0.4-1.5)		0.8 (0.4-1.7)			
Gender	Female	20	10	ref	0.164	ref	0.129	ref	0.107
	Male	94	62	1.6 (0.8-3.1)		1.9 (0.8-4.4)		1.7 (0.9-3.4)	
Age	Per 5 years	11							
		4	72	1.1 (1.0-1.2)	0.079	1.2 (1.0-1.4)	0.071	1.1 (1.0-1.3)	0.044
T stage	Per 1 stage increase	11							
		4	72	1.0 (0.8-1.2)	0.940	1.2 (0.9-1.6)	0.273	1.1 (0.9-1.5)	0.375
N stage	Per 1 stage increase	11							
		4	72	1.0 (0.9-1.3)	0.660	1.3 (1.0-1.8)	0.083	1.2 (1.0-1.6)	0.109
ECOG	Per unit increase	11							
		4	72	1.4 (1.1-1.8)	0.018	1.3 (0.9-1.8)	0.136	1.3 (1.0-1.7)	0.087
ACE27	Per unit increase	11							
		4	72	1.4 (1.1-1.8)	0.005	1.4 (1.1-1.8)	0.018	1.3 (1.0-1.6)	0.047
Smoking	Never								
	smoked	7	4	ref	0.295	ref	0.967		
	Current or ex-	10	65	1.7 (0.6-4.8)		1.0 (0.2-3.9)			

	smoker	3					
Concurrent chemotherapy	No	46	32	ref	0.171	ref	0.997

Table 3. Patient and tumour characteristics by ACE-27

Variable	Level	ACE27 score 0-1	ACE27 score 2-3
ECOG	0	14 (25.9%)	15 (25.0%)
	1	30 (55.6%)	23 (38.3%)
	2	8 (14.8%)	17 (28.3%)
	3	2 (3.7%)	5 (8.3%)
T stage	1	10 (18.5%)	10 (16.7%)
	2	7 (13.0%)	17 (28.3%)
	3	10 (18.5%)	13 (21.7%)
	4	27 (50.0%)	20 (33.3%)
N stage	0	30 (55.6%)	28 (46.7%)
	1	4 (7.4%)	6 (10.0%)
	2A	1 (1.9%)	1 (1.7%)
	2B	2 (3.7%)	9 (15.0%)
	2C	11 (20.4%)	7 (11.7%)
	3	6 (11.1%)	9 (15.0%)
EQD2 (Gy)	15.75	0 (0.0%)	1 (1.7%)
	66	0 (0.0%)	2 (3.3%)
	66.21	4 (7.4%)	11 (18.3%)
	67.31	9 (16.7%)	8 (13.3%)
	70	34 (63.0%)	28 (46.7%)
	70.2	7 (13.0%)	10 (16.7%)
Subsite	Glottis	20 (37.0%)	24 (40.0%)
	Hypopharynx	5 (9.3%)	9 (15.0%)
	Oral cavity	8 (14.8%)	6 (10.0%)
	Oropharynx	9 (16.7%)	11 (18.3%)
	Supraglottis	12 (22.2%)	10 (16.7%)
Completed Treatment	No	2 (3.7%)	5 (8.3%)
	Yes	52 (96.3%)	55 (91.7%)

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