Age alone is not a barrier to concurrent chemoradiotherapy for advanced head and neck cancer

Objectives

To evaluate the benefits imparted by concurrent chemoradiotherapy (CCRT) and chemotherapy of any form to elderly head and neck cancer (HNC) patients in Ireland. Secondary outcomes included comparison of these benefits to the adult population and subgroup analysis by site.

Design, setting, and participants

A retrospective cohort study was conducted using 20 years of cancer registry data provided by the National Cancer Registry of Ireland. All HNC diagnosed from 1994-2014 were included. Cox multivariate regression analysis was applied to test for the benefits of CCRT and chemotherapy of any form in HNC. The primary outcome measures were cancer-specific and all-cause survival in months.

Results

Survival analysis showed an overall benefit to the use of CCRT in patients with advanced disease over 65 years, particularly when used for hypopharyngeal, oral cavity, oropharyngeal, and laryngeal malignancy, though the latter did not achieve statistical significance. Chemotherapy of any form conferred a survival benefit in elderly patients with hypopharyngeal, laryngeal, nasopharyngeal, and oropharyngeal cancer.

Conclusion

CCRT and chemotherapy of any form confer significant survival benefits to appropriately selected elderly HNC patients and should therefore not be withheld solely on the basis of age.

Keywords

Head and neck cancer; elderly; concurrent chemoradiotherapy; chemotherapy; survival

Key Points

- Concurrent chemoradiotherapy improves survival in selected groups of head and neck cancer patients including elderly patients.
- Specific head and neck cancer subtypes which derive benefit include hypopharyngeal, oral cavity, oropharyngeal, and laryngeal malignancies.
- There continues to be a survival benefit to concurrent chemoradiotherapy over 65 years of age.
- Chemotherapy of any form improves survival in elderly patients.
- Very few patients over 75 years receive combined modality treatment.

Introduction

Up to 70% of Head and Neck Cancer (HNC) presents with either locoregionally advanced or metastatic disease [1], with only 30% achieving cure despite intensive multi-modality therapy [2]. Primary chemotherapy has long been shown to improve the response of HNC to definitive surgery or radiotherapy [3, 4]. Concurrent chemoradiotherapy (CCRT) is a treatment modality of choice in advanced disease, offering equivalent locoregional control and survival to surgery in selected patients [5-7]. The most crucial determinant of optimal therapy in advanced disease is the primary site – oral cavity malignancies are often most amenable to surgical resection, whereas pharyngeal malignancies are often best managed with primary radiotherapy [8, 9].

The optimal regime in the elderly population remains in doubt due to their under-representation in clinical trials [10]. A recent retrospective cohort study concluded combining chemotherapy with local therapy offers diminishing benefits with advancing age [11]. Conversely, other observational data contend that combined chemoradiotherapy should not be withheld solely on the basis of age, as those with good functional reserve may still derive benefit [5].

There is a paucity of data published with the aim of examining the benefit of chemotherapy in elderly patients.

Objectives

The primary objective of this study was to examine the survival benefit imparted by CCRT compared to radiotherapy alone in elderly locoregionally advanced HNC patients with comparison to the adult population. Secondary outcomes included the survival benefit imparted by any chemotherapy and subgroup analysis for survival benefit by site.

Methods

Study Design

A retrospective cohort study was conducted using STROBE standardised reporting guidelines. The study cohort was derived from a database derived from electronic healthcare records and physical charts maintained by the National Cancer Registry

of Ireland (NCRI) of HNC patients in Ireland between 1994 and 2014 [12]. The length of cancer-specific follow-up was until the end of 2015. The data that support the findings of this study are available from NCRI. Restrictions apply to the availability of these data, which were used under license for this study. Data are available from the authors with the permission of NCRI.

Inclusion/Exclusion Criteria

The sole inclusion criterion was patients with HNC (as defined by TNM 8th Edition [13]) diagnosed within the period specified. The primary exclusion criteria were patients with cancers occurring outside this definition, and cutaneous and thyroid cancers.

Variables

The outcome variables were time to cancer-specific and all-cause mortality. The exposure variables were treatment modalities utilised, either CCRT or chemotherapy. Descriptive variables included gender, age, primary site, histology, TNM classification and stage as per American Joint Committee on Cancer (AJCC). Also included was time in days from diagnosis to treatment commencement for each modality. The primary confounder was comorbidity of the patient population, for which the database includes no data. All data were sourced from NCRI.

Statistical Methods

Descriptive statistics for participants' baseline characteristics were generated. 643 patients presenting in 2014 were excluded from survival analysis due to incomplete staging data. Kaplan-Meier survival analysis was conducted to test the survival benefit of CCRT compared with radiotherapy alone overall, to patients over 65 years (hereafter referred to as the 'elderly' cohort), and those under 65 years (hereafter referred to as the 'adult' cohort) who presented with locoregionally advanced disease, defined as stage III, IVA, or IVB. This analysis was also performed for chemotherapy compared with no chemotherapy for locoregionally advanced or metastatic (stage IVC) disease. Hazard ratios adjusted for gender, year of incidence, site, histology, and stage as categorical variables were generated using multivariate Cox analysis. These results were further interrogated by dividing the population into elderly and adult cohorts. Differences between the cohorts was assessed statistically

with an interaction term. These analyses were repeated upon site groupings separately.

Statistical analyses were conducted using Stata version 16.1. Statistical significance was assumed at $p<0.05$.

Ethical Considerations

Ethical approval was sought from and approved by <blinded for review>. The database already existed, and NCRI retains legislative authority to license data analysis for research purposes [14]. The authors have no conflicts of interest to declare.

Results

Baseline characteristics

10148 patients were identified. Baseline characteristics are summarised in Table 1. Elderly patients comprised 48.1% (n=4886). The predominant histopathological diagnosis was squamous cell carcinoma (84.3%, n=8555).

The 18 sites and 79 subsites reported were grouped anatomically according to AJCC standards [15] as shown in Table 1. Sites overlapping these groups or lesions without definite anatomical location were designated “other” (n=366, 3.6%) and excluded from survival analysis. The oral cavity was the most common site (29.8%, n=3028) followed by the larynx (28.1%, n=2848) and oropharynx (15.8%, 1606).

Stage statistics organised by site are summarized in Table 2. 30.3% (n=3075) presented with stage 0, I or II disease. Stage III disease was present in 10.9% (n=1102), non-metastatic stage IV disease was present in 24.3% (n=2469), and stage IVC disease was present in 3.9% (393). 30.8% (n=3109) had no record of stage (stage X).

Treatment groups are summarised in Tables 3 and 4. 739 patients with locoregionally advanced disease underwent CCRT compared with 1584 who underwent radiotherapy alone. 217 (29.3%) of the CCRT cohort were elderly. 35.2% (N=1396) of patients with locoregionally advanced or metastatic disease received chemotherapy.

Survival Analysis

The results of adjusted Cox regression multivariate analysis for the effect of treatment regimens overall and stratified by age are summarised in Table 5. The p-values from an interaction term between the age groups are also shown.

CCRT conferred improved cancer-specific survival over radiotherapy alone for locoregionally advanced HNC (HR 0.60, 95% CI 0.52, 0.70). There was no statistically significant difference between the benefit imparted to elderly and adult patients (p=0.699).

Chemotherapy conferred improved cancer-specific survival in locoregionally advanced or metastatic HNC (HR 0.83, 95% CI 0.75-0.91). This benefit was not observed for cancer-specific (HR 0.98, 95% CI 0.87-1.11) or all-cause mortality (HR 1.03, 95% CI 0.93-1.15) in adult patients, but was observed in elderly patients (HR 0.67, 95% CI 0.57-0.78). The difference in effect was highly statistically significant (p=0.0001).

Subgroup analysis was performed for patients over 70 and 75 years with locoregionally advanced disease. There was a benefit to CCRT over radiotherapy alone for cancer-specific mortality in patients over 70 years (HR 0.65, 95% CI 0.47-0.88). There was no statistically significant benefit to CCRT over radiotherapy alone for cancer-specific (HR 0.8, 95% CI 0.47-1.34) or all-cause mortality (HR 1, 95% CI 0.68-1.51) in patients over 75 years. This group included 38 who received CCRT and 667 who received radiotherapy.

Survival Analysis by Site

The results of site-specific survival analyses for cancer-specific mortality are summarised in Table 6.

Hypopharynx

CCRT conferred improved cancer-specific survival over radiotherapy alone in elderly patients with locoregionally advanced hypopharyngeal cancer (HR 0.52, 95% CI 0.33-0.82). This was not observed in adult patients (HR 1.19, 95% CI 0.77-1.84). There was no statistically significant difference between these effects (p=0.119).

Chemotherapy conferred improved cancer-specific survival in elderly patients with locoregionally advanced or metastatic hypopharyngeal cancer (HR 0.49, 95% CI 0.36-0.69). This was not observed in adult patients (HR 1.13, 95% CI 0.83-1.54). The difference between these effects was statistically significant (p=0.001).

Larynx

CCRT conferred improved cancer-specific (HR 0.66, 95% CI 0.43-1.01, p=0.053) and all-cause survival (HR 0.66, 95% CI 0.47-0.91, p=0.012) over radiotherapy alone in elderly patients with locoregionally advanced laryngeal cancer. This was also observed in adult patients (HR 0.52, 95% CI 0.35-0.77). There was no statistically significant difference between these effects (p=0.799).

Chemotherapy conferred improved cancer-specific survival in elderly patients with locoregionally advanced or metastatic laryngeal cancer (HR 0.65, 95% CI 0.47-0.89). This did not achieve statistical significance in adult patients (HR 0.94, 95% CI 0.74-1.19). The difference between these effects was statistically significant (p=0.017).

Nasal Cavity & Paranasal Sinuses

CCRT conferred improved cancer-specific survival over radiotherapy alone for patients with locoregionally advanced nasal cavity and paranasal sinus (NCPS) cancer (HR 0.31 95% CI 0.116-0.825, p=0.02). There was insufficient cases to analyse age groups separately. Chemotherapy conferred no identifiable benefit for NCPS cancer.

Nasopharynx

CCRT conferred a statistically non-significant increase in cancer-specific mortality compared to radiotherapy alone in elderly patients with locoregionally advanced nasopharyngeal cancer (HR 1.94, 95% CI 0.50-7.51, p=0.339), but improved survival in adult patients (HR 0.38, 95% CI 0.17-0.84). The difference between these effects did not achieve statistical significance (p=0.11).

Chemotherapy conferred improved cancer-specific survival (HR 0.35, 95% CI 0.14-0.87) to elderly patients with locoregionally advanced or metastatic nasopharyngeal cancer. This benefit was not statistically significant in adult patients (HR 0.64, 95% CI 0.38-1.08). The difference between these effects was not statistically significant (p=0.104).

Oral Cavity

CCRT conferred improved cancer-specific survival over radiotherapy alone for elderly (HR 0.48, 95% CI 0.23-1.00, p=0.05) and adult (HR 0.45, 95% CI 0.28-0.74) patients with locoregionally advanced oral cavity cancer. The difference between these effects was not statistically significant (p=0.949).

Chemotherapy conferred no benefit to cancer-specific (HR 0.82, 95% CI 0.58-1.16) or all-cause mortality (HR 0.77, 95% CI 0.57-1.04) in elderly patients with locoregionally advanced oral cavity cancer. Chemotherapy increased cancer-specific (HR 1.23, 95% CI 0.97-1.56, p=0.089) and all-cause mortality (HR 1.21, 95% CI 0.98-1.50) in adult patients, though this did not achieve statistical significance. The difference between these groups was statistically significant (p=0.03).

Oropharynx

CCRT conferred improved cancer-specific survival over radiotherapy alone in elderly (HR 0.42, 95% CI 0.28-0.64) and adult (HR 0.47, 95% CI 0.34-0.64) patients with locoregionally advanced oropharyngeal cancer. The difference between these effects was not statistically significant (p=0.623).

Chemotherapy conferred improved cancer-specific survival in elderly (HR 0.56, 95% CI 0.42-0.74) and adult (HR 0.59, 95% CI 0.48-0.74) patients with locoregionally advanced or metastatic oropharyngeal cancer. The difference between these effects was not statistically significant (p=0.682).

Salivary Glands

There was no statistically significant benefit to cancer-specific or all-cause mortality associated with CCRT or chemotherapy for advanced salivary gland cancer.

Discussion

Table 5 shows that elderly Irish patients with locoregionally advanced HNC derived survival benefit from CCRT. Above the age of 75 there appears to be no identifiable benefit. There were, however, only 38 patients in the CCRT arm of this group and it remains difficult to draw definite conclusions about CCRT for the very elderly.

Chemotherapy for locoregionally advanced or metastatic disease demonstrated benefit in the elderly but not the adult population. It is hypothesised this occurred due to chemotherapy being more liberally employed in younger patients, resulting in a heterogeneous population comprising both palliative and curative intent. In the elderly, chemotherapy risks increased toxicity for little perceived benefit to quality or length of life. As such, elderly patients who underwent chemotherapy likely represent the ‘fit elderly’ group for whom intensive therapy offers sufficient perceived benefit to outweigh the risks. A subject of ongoing interest is the development of a systematic means of identifying the fit elderly patient. The currently recommended approach

consists of clinical assessment coupled with screening tools for risk stratification of patients requiring geriatric review [16].

The primary confounders in this study are the comorbid nature of this population, disease progression, and response to therapy. It is likely those considered candidates for CCRT were generally less comorbid than those who received radiotherapy alone, which may partially account for observed differences. Disease progression is a key prognostic indicator for HNC, as locoregional or distant recurrence indicates disease likely to be poorly responsive to salvage treatment. Response to therapy is of particular interest for CCRT; many protocols assess response during treatment, with non-responders considered for salvage under the assumption that further organ-preserving treatment will be futile. The data presented cannot systematically account for this eventuality.

Hypopharynx

There was no benefit to CCRT over radiotherapy alone or to chemotherapy for adults with advanced hypopharyngeal cancer. By contrast, there were strong benefits to both CCRT and chemotherapy in the elderly population. The groups had approximately equal numbers (347 under 65, 390 over 65), though a higher proportion of adult patients received CCRT than did elderly patients (27% vs 13%). There may again be inherent biases that promote the use of chemotherapy more liberally in the younger, ‘fitter’ patient in pursuit of definite cure resulting in a more heterogeneous cohort in this group relative to the elderly group, where the use of chemotherapy must be considered carefully. The data support the use of CCRT and chemotherapy for elderly advanced hypopharyngeal cancer patients.

Larynx

CCRT conferred a clear survival benefit over radiotherapy alone in the adult population with laryngeal cancer. In the elderly cohort, there was also benefit to survival but this only reached statistical significance for all-cause mortality. The use of any chemotherapy nonetheless imparted a clear survival benefit to elderly patients, though, similar to the hypopharyngeal malignancy cohort, this effect was not replicated in the adult population. There are again likely to be multiple confounders at play leading to the difference noted here. The data support the use of CCRT and chemotherapy for elderly advanced laryngeal cancer patients.

Nasopharynx

Radiotherapy and CCRT are considered standard of care for early and advanced nasopharyngeal malignancy [17, 18]. Despite this, CCRT conferred benefit in the adult population but not in the elderly. There was nonetheless a statistically significant survival benefit imparted by chemotherapy in the elderly; a similar benefit was observed in the adult population but failed to achieve statistical significance. This suggests that chemotherapy confers benefit in the elderly but may not be being used in the form of CCRT. Given the undisputed role of CCRT in nasopharyngeal cancer management, the lack of identifiable benefit in the elderly likely reflects the heterogeneous nature of a malignancy which is rare in Ireland. It furthermore reflects the importance of such cases being managed in a centre of excellence for HNC.

Oral Cavity

CCRT demonstrated superiority over radiotherapy alone in both adult and elderly patients with oral cavity cancer, which reflects the use of CCRT as the primary option in unresectable disease [19, 20]. There was no evidence of benefit associated with chemotherapy overall; indeed, there was a nearly statistically significant increase in mortality associated with chemotherapy in the adult population. This may reflect the high recurrence rate in oral cavity cancer, and the benefit of chemotherapy failing to outweigh the increased mortality associated with recurrent disease. The data support the use of CCRT in elderly oral cavity cancer patients.

Oropharynx

Oropharyngeal cancer has been the object of significant interest over the last 30 years as the pathophysiological impact of HPV infection has become apparent [21]. The use of CCRT has shown benefit in terms of both survival and morbidity for advanced disease [22], and the Irish data is congruent. The use of any chemotherapy was also associated with improved survival, reflecting the key role that systemic therapy plays in advanced oropharyngeal cancers. The data support the use of CCRT and chemotherapy for elderly oropharyngeal cancer patients.

Conclusion

CCRT and chemotherapy are valuable tools in the armamentarium of HNC physicians, offering improved survival to selected patients with hypopharyngeal,

laryngeal, oral cavity, and oropharyngeal malignancies. Questions remain as to how best to select candidates for intensive therapy from an ageing population, but registry data demonstrates that chemotherapy should not be withheld from elderly patients on the basis of age alone.

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Table 1 - Baseline characteristics of Irish head & neck cancer patients 1994-2014

Variable	Frequency	Percentage	Cumulative %
Age Group			
00_04	11	0.11	0.11
05_09	12	0.12	0.23
10_14	23	0.23	0.45
15_19	33	0.33	0.78
20_24	30	0.3	1.07
25_29	46	0.45	1.53
30_34	106	1.04	2.57
35_39	161	1.59	4.16
40_44	297	2.93	7.09
45_49	649	6.4	13.48
50_54	990	9.76	23.24
55_59	1,375	13.55	36.79
60_64	1,529	15.07	51.85
65_69	1,441	14.2	66.05
70_74	1,270	12.51	78.57
75_79	997	9.82	88.39
80_84	674	6.64	95.03
85+	504	4.97	100
Year Of Incidence			
1994	434	4.28	4.28
1995	431	4.25	8.52
1996	417	4.11	12.63
1997	405	3.99	16.62
1998	427	4.21	20.83
1999	397	3.91	24.74
2000	414	4.08	28.82
2001	319	3.14	31.97
2002	440	4.34	36.3
2003	422	4.16	40.46
2004	452	4.45	44.92

Variable	Frequency	Percentage	Cumulative %
2005	468	4.61	49.53
2006	482	4.75	54.28
2007	489	4.82	59.1
2008	504	4.97	64.06
2009	536	5.28	69.34
2010	603	5.94	75.29
2011	603	5.94	81.23
2012	601	5.92	87.15
2013	661	6.51	93.66
2014	643	6.34	100
Gender			
F	2,623	25.85	25.85
M	7,525	74.15	100
Histology			
Adenocarcinoma	631	6.22	6.22
Melanoma	61	0.6	6.82
Unspecified	825	8.13	14.95
Sarcoma	76	0.75	15.7
Squamous Cell Carcinoma	8,555	84.3	100
Site			
Hypopharynx	793	7.81	7.81
Larynx	2,848	28.06	35.88
Nasal cavity / Paranasal sinuses	482	4.75	40.63
Nasopharynx	305	3.01	43.63
Oral cavity	3,028	29.84	73.47
Oropharynx	1,606	15.83	89.3
Other	366	3.61	92.91
Salivary gland	720	7.09	100

Table 2 – Overall and stratified by site statistics on disease stage at presentation

Key									
Frequency									
Row percentage									
Stage	Hypopharynx	Larynx	Nasal Cavity / Paranasal Sinuses	Nasopharynx	Oral Cavity	Oropharynx	Other	Salivary Gland	Total
0	0	4	0	0	0	0	1	0	5
	0	0.14	0	0	0	0	0.27	0	0.05
I	15	753	3	8	791	110	39	142	1,861
	1.89	26.44	0.62	2.62	26.12	6.85	10.66	19.72	18.34
II	47	514	15	24	395	119	45	50	1,209
	5.93	18.05	3.11	7.87	13.04	7.41	12.3	6.94	11.91
III	76	384	21	32	308	215	38	28	1,102
	9.58	13.48	4.36	10.49	10.17	13.39	10.38	3.89	10.86
IV	228	480	50	36	741	697	117	120	2,469
	28.75	16.85	10.37	11.8	24.47	43.4	31.97	16.67	24.33
IVC	48	97	6	28	84	104	26	0	393
	6.05	3.41	1.24	9.18	2.77	6.48	7.1	0	3.87
X	379	616	387	177	709	361	100	380	3,109
	47.79	21.63	80.29	58.03	23.41	22.48	27.32	52.78	30.64
Total	793	2,848	482	305	3,028	1,606	366	720	10,148
	100	100	100	100	100	100	100	100	100

Table 3 – CCRT vs RT treatment groups by site and age group for locoregionally advanced disease

Group	CCRT	RT	Total
Hypopharyngeal			
Adult	79	75	154
Elderly	45	142	187
Total	124	217	341
Laryngeal			
Adult	106	226	332
Elderly	66	279	345
Total	172	505	677
Nasal Cavity			
Adult	13	20	33
Elderly	8	61	69
Total	21	81	102
Nasopharyngeal			
Adult	45	42	87
Elderly	6	27	33
Total	51	69	120
Oral Cavity			
Adult	51	82	133
Elderly	16	161	177
Total	67	243	310
Oropharyngeal			
Adult	201	165	366
Elderly	66	140	206
Total	267	305	572
Other			
Adult	24	36	60
Elderly	9	45	54
Total	33	81	114
Salivary Gland			
Adult	3	26	29
Elderly	1	57	58
Total	4	83	87

Table 4 – Chemotherapy treatment groups by site and age group for locoregionally advanced or metastatic disease

Group	Chemotherapy	No Chemotherapy	Total
Hypopharyngeal			
Adult	109	66	175
Elderly	63	114	177
Total	172	180	352
Laryngeal			
Adult	209	313	522
Elderly	93	359	452
Total	302	672	974
Nasal Cavity			
Adult	19	21	40
Elderly	10	27	37
Total	29	48	77
Nasopharyngeal			
Adult	57	10	67
Elderly	9	20	29
Total	66	30	96
Oral Cavity			
Adult	190	398	588
Elderly	57	462	519
Total	247	860	1107
Oropharyngeal			
Adult	382	304	686
Elderly	114	229	343
Total	496	533	1029
Other			
Adult	43	53	96
Elderly	14	71	85
Total	57	124	181
Salivary Gland			
Adult	13	46	59
Elderly	14	75	89
Total	28	121	149

Table 5 - Effect of treatment regimens on cancer-specific and all-cause mortality overall and stratified by age with interaction term

Treatment Regime	Adjusted HR (95%CI)	Age <65 Adjusted HR (95%CI)	Age>=65 Adjusted HR (95%CI)	P-value for the interaction term between age groups
Cancer-specific survival				
CCRT vs RT alone	0.60 (0.52-0.70)	0.61 (0.50-0.74)	0.60 (0.48-0.76)	0.699
Chemo vs no chemo	0.83 (0.75-0.91)	0.98 (0.87-1.11)	0.67 (0.57-0.78)	0.001
Overall survival				
CCRT vs RT	0.69 (0.61-0.78)	0.72 (0.61-0.85)	0.66 (0.54-0.79)	0.774
Chemo vs no chemo	0.89 (0.82-0.96)	1.03 (0.93-1.15)	0.74 (0.65-0.83)	<0.001

CCRT – Concurrent Chemoradiotherapy. RT – Radiotherapy. Chemo – Chemotherapy.

Table 6 – Effect of treatment regimens on cancer-specific mortality by site stratified by age with interaction term

Site Treatment Regime	**Age<65 Adjusted HR (95%CI)**	**Age>=65 Adjusted HR (95%CI)**	**P-value for interaction term**
Hypopharynx			
CCRT vs RT alone	1.19 (0.77-1.84)	0.52 (0.33-0.82)	0.119
Chemo vs no chemo	1.13 (0.83-1.54)	0.49 (0.36-0.69)	0.001
Larynx			
CCRT vs RT alone	0.52 (0.35-0.77)	0.66 (0.43-1.01)	0.799
Chemo vs no chemo	0.94 (0.74-1.19)	0.65 (0.47-0.89)	0.017
Nasal Cavity / Paranasal Sinuses			
CCRT vs RT alone	0.31 (0.05-1.78)	0.21 (0.03-1.56)	0.357
Chemo vs no chemo	1.06 (0.56-2.02)	1.23 (0.62-2.44)	0.804
Nasopharynx			
CCRT vs RT alone	0.38 (0.17-0.84)	1.94 (0.50-7.51)	0.11
Chemo vs no chemo	0.64 (0.38-1.08)	0.35 (0.14-0.87)	0.104
Oral Cavity			
CCRT vs RT alone	0.45 (0.28-0.74)	0.48 (0.23-1.00)	0.949
Chemo vs no chemo	1.23 (0.97-1.56)	0.82 (0.58-1.16)	0.03
Oropharynx			
CCRT vs RT alone	0.47 (0.34-0.64)	0.42 (0.28-0.64)	0.623
Chemo vs no chemo	0.59 (0.48-0.74)	0.56 (0.42-0.74)	0.682
Salivary Glands			
CCRT vs RT alone	0.71 (0.12-4.30)	3.66 (0.41-32.28)	0.597
Chemo vs no chemo	1.84 (0.87-3.87)	0.89 (0.44-1.82)	0.048

CCRT – Concurrent Chemoradiotherapy. RT – Radiotherapy. Chemo – Chemotherapy.