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Oropharyngeal Cancer (OPC) Drives Racial Outcome Disparities in Squamous Cell Carcinoma of the Head and Neck (HNSCC): Ten Year Experience at the University of Maryland Greenebaum Cancer Center (UMGCC)

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Abstract

Background—Racial outcome disparities have been observed in HNSCC with diminished survival for black patients compared to whites.

Methods—We retrospectively analyzed 1318 patients with primary HNSCC treated at the UMGCC from 2000 to 2010.

Results—65.9% were white, 30.7% were black and 3.3% were of other races. Blacks were less likely to present with oral cavity cancer (OC), and more likely to present with laryngeal or hypopharyngeal cancers. Whites were more likely to have early stage disease, especially in the OC. Black race was independently associated with worse OS in the entire cohort. Blacks had a significantly worse OS amongst OC and oropharyngeal cancers (OPC), with the largest disparity in OPC. However in multivariate analysis race was only still significant in OPC.

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Conclusion—We observed differences by race in distribution of disease site, stage, and OS. Survival disparity in the entire cohort was driven mostly by differences amongst OPC.

Keywords

Race; HNSCC; Oropharyngeal; Survival; Disparity

Introduction

Squamous cell carcinoma of the head and neck (HNSCC) includes cancers that originate in the oral cavity, oropharynx, hypopharynx, and larynx. Worldwide HNSCC is the 6th most common cancer¹, and it estimated that in 2013 there will be a total of 53,640 new cases of oral cavity, laryngeal and pharyngeal cancer diagnosed in the United States.² Traditional risk factors for HNSCC include smoking and alcohol; however additional research over the last three decades has shown that the human papillomavirus (HPV) has an etiological role in the development of squamous cell carcinoma of the oropharynx (OPSCC), with predilection for tumors involving the tonsils or base of tongue.^{3, 4} Importantly, HPV positive oropharyngeal cancers are more responsive to treatment with improved survival.⁵⁻⁸

Race-based differences in disease characteristics, referral patterns, treatments and outcomes are observed in a number of malignancies, including prostate cancer^{9, 10}, breast cancer^{11, 12}, and acute myeloid leukemia¹³⁻¹⁵. Disparities between black and white patients are also seen in HNSCC. Compared to whites, black patients have a higher incidence rate of HNSCC,^{16, 17} and are diagnosed at a younger age.¹⁸⁻²⁰ They are more likely to have a history of tobacco and alcohol exposure,^{21, 22} present at a more advanced stage of disease,^{20, 22, 23} and are more likely to undergo non operative treatment^{23, 24}. Worse outcomes including in disease specific survival and overall survival are seen in black patients even after controlling for baseline characteristics including stage and treatment²⁵⁻²⁷. Additionally recent analysis pioneered by studies from our group, demonstrate remarkable disparities in the prevalence of HPV positive OPSCC between black and white patients²⁸⁻³¹. The higher prevalence of HPV positive OPSCC in whites and the associated improved prognosis may partially explain overall differences in survival by race.^{29, 32}

Most of the analysis on racial disparities in HNSCC comes from tumor registries spanning multiple centers. Therefore, we retrospectively analyzed HNSCC patients treated at the University of Maryland Greenebaum Cancer center (UMGCC) between 2000 and 2010, to determine whether differences exist in baseline characteristics and survival between black and white HNSCC patients.

Materials and Methods

Following IRB approval we performed a retrospective chart review of data from patients treated at UMGCC for HNSCC from 2000 to 2010. We identified cases with biopsy proven squamous cell carcinoma of the oropharynx, oral cavity, larynx, or hypopharynx treated for a first primary diagnosis. Data collected included race, gender, age at diagnosis, smoking status, alcohol use, tumor stage, nodal stage, overall staging, treatment received, and year of diagnosis. Race as well as tobacco smoking and alcohol status of patients was self reported.

TNM staging (www.nccn.org) was used to define tumor, nodal and overall staging. Any missing values were recorded as unknown.

Statistical Consideration

This retrospective statistical analysis was conducted using records on the 1318 GCC patients. Patients' demographic and clinical on-study characteristics were summarized and compared between two ethnic groups, i.e., Black and White patients, for entire cohort and within a cancer site. The Fisher's and Fisher-Freeman-Halton's tests for categorical variables and the GLM approach for continuous variables were utilized. Corresponding to these tests probabilities were either two-sided exact or calculated with the use of Monte Carlo simulations.¹ OS was defined from the date of diagnosis till the date of death from any cause or censored at the date last known alive. OS functions were estimated and compared using the Kaplan-Meier approach and the log-rank tests, respectively. Median OS times with the corresponding 95% confidence intervals (CI) were calculated. The univariable and multivariable Cox regression models were applied to identify plausible predictors as well as the magnitude of their effect on survival parameters (HR, hazard of death). All statistical tests were done at 0.05 Type I error. Statistical analyses were conducted using S-plus (TIBCO, v. 8.2) and SAS (SAS Institute Inc, Cary, NC, v.9.3).

Results

A total of 1318 patients with first primary oral cavity, oropharyngeal, laryngeal or hypopharyngeal tumors treated at UMGCC were identified between 2000 and 2010. Racial distribution included 65.9% (869) white, 30.7% (405) black, and 3.3% (44) other races. The median age of the entire population was 60, and patients were predominantly male (72.7%). Breakdown by anatomic site included 43.2% (570) oral cavity, 28.3% (373) oropharynx, 23.6% (311) larynx, and 4.9% (64) hypopharynx. (Table 1) Compared to all white patients, black patients differed in gender distribution with a higher percentage of males (76.5%), and were more likely to have a history of smoking or alcohol or combined smoking and alcohol. Whites and blacks differed significantly in TNM staging at presentation and treatments received, with blacks having a higher percentage of locally advanced disease (stage III/IVa/IVb) and being treated with chemoradiation or radiation alone versus the majority of white patients who were treated with surgery (Table 2). By primary site, there was a significant difference in treatment between black and white patients with oral cavity, oropharynx, and hypopharyngeal cancers but not for patients with cancers of the larynx (supplemental Table 5). Ninety six percent of oral cavity cancer patients underwent surgery accounting for the largest number of patients treated with surgical resection, and the largest disparity in surgical treatment where 77% of white and 61% of black oral cavity patients were treated with surgery alone.

There were also significant differences in racial distribution between primary sites. (Table 3) While blacks made up 30.7% of our HNSCC population overall, blacks accounted for 65.6% of hypopharyngeal, 47.9% of laryngeal, and 33.5% of oropharyngeal cancers. The largest disparity between races was in oral cavity cancers where blacks accounted for 15.6% of patients while whites accounted for 79.3%. Smoking and alcohol status as well as stage

differed significantly between primary site with the largest percentage of smokers in laryngeal primaries and both alcohol users and smokers amongst cancers in the hypopharynx. The greatest proportion of early stage (stage I and II) diagnosis were amongst patients with oral cavity tumors, with the largest percentage of locally advanced cases amongst oropharyngeal and hypopharyngeal cancers.

Survival analysis (Table 4, Figures 1 and 2) for our entire population showed a significantly worse overall survival for all black patients compared to white (median 2.5 years vs. 4.8 years, respectively, $p < 0.0001$) (Figure 1). By primary site, blacks had a significantly worse OS compared to whites for both oropharyngeal (median 4.9 vs. 2.1 years respectively, $p < 0.0001$) (Figure 2A) and oral cavity tumors (median 5.7 vs. 3.2 years respectively, $p < 0.0001$) (Figure 2B). There was no difference in OS between blacks and whites for both laryngeal and hypopharyngeal cancers (Figures 2C and 2D respectively).

In order to evaluate the effect of relevant baseline characteristics including race, age, gender, smoking and alcohol status, and stage on overall survival, we conducted a multivariable regression analysis for the entire cohort of HNSCC patients as well as by individual primary site. For all patients overall survival was independently affected by all of these characteristics (as well as primary site) except for gender, with the hazard of death in black patients 1.2 times that of whites (Table 5). While blacks had worse survival than whites in the oral cavity, in multivariable Cox regression model, race no longer had a significant effect on survival (Supplemental Table 2). However amongst oropharyngeal cancer patients race was still a strongly associated with worse outcome with blacks having a risk of death 1.6 times that of whites even after controlling for gender, age, smoking and alcohol, and stage (Table 6). Amongst laryngeal cancer patients OS survival was effected by age and stage of disease (Supplemental Table 3), while amongst hypopharyngeal patients no risk factors associated with overall survival were identified (Supplemental Table 4).

Discussion

In our retrospective analysis of 1318 patients with HNSCC treated at UMGCC from 2000-2010 we found that blacks had a significantly worse overall survival than white patients including after controlling for age, gender, tobacco and alcohol use, stage, and primary site. By primary site black patients with oral cavity and oropharyngeal cancers fared worse than whites. However after including the aforementioned baseline characteristics in a multivariate model, black race was associated with worse outcome only amongst oropharyngeal primaries.

In analysis of our entire patient population, blacks were younger, had a higher male predominance, were more likely to use tobacco and alcohol, and present at a more advanced stage compared to white patients. These findings are similar to what has been reported in the literature.¹⁸⁻²² For example, analysis of 1,128 HNSCC patients using a tumor registry in the southern united states, showed that a significantly higher percentage of black patients were diagnosed before the age of 50 (33.9% vs. 25.1% respectively).²⁰ Reasons for blacks presenting at a younger age are unclear but may have to do with smoking and drinking patterns, both of which are significant risk factors for HNSCC.^{18,33} Blacks have repeatedly

been observed to present at a more advanced stage than whites.^{20, 34-36} While reasons for presentation at a later stage are complex, including various socioeconomic factors, data from a cohort study involving patients with oral cavity and laryngeal cancers treated at the University of Pittsburgh found that blacks presented at a more advanced stage even after matching for smoking and age, and adjusting for socioeconomic status and insurance.³⁵

In our univariate survival analysis by primary site, blacks with both oral cavity and oropharyngeal tumors had a significantly inferior overall survival compared to whites with a greater disparity in outcome amongst the oropharynx. Multivariate analysis showed that after controlling for gender, age, stage and tobacco and alcohol, black race was associated with worse outcome amongst oropharyngeal cancer patients, while it was not a significant predictor of outcome for patients with oral cavity tumors. No difference in survival by race was seen amongst laryngeal or hypopharyngeal cancer patients.

In our institutional experience, we observed striking differences in the racial and gender distribution of patients by disease site. The largest disparity between numbers of black and white patients occurred in the oral cavity where patients were predominantly white. While by SEER data, reported age adjusted incidence rates per 100,000 patients from 2006-2010 showed a higher age adjusted incidence for white patients compared to black amongst cancers of the tongue (3.4 vs. 2.2, respectively) and lip (0.8 vs. 0.1, respectively) there were no differences at all other sites in the oral cavity (www.seer.cancer.gov). By gender, the oral cavity had the highest percentage of female patients (30%) with a striking difference by race, where 80% females were white and only 15% were black. In no other primary site was there such a large disparity in racial distribution of female patients. Indeed, in analysis of SEER data over the past four decades, the incidence of oral cavity cancers have been increasing in younger women over time. This increase has been driven specifically by an increasing incidence of oral tongue cancers in white women, while the incidence has been decreasing in black women.^{37, 38} For example, while the overall incidence of oral tongue cancer decreased by 4% between 1975 and 2007, with a 55% decrease in black women, the incidence increased by 21% in all white women, with a striking 111% increase in younger white women ages 18-44.³⁸ The reason for a rise in incidence of oral cavity cancers amongst white women is unclear and requires further investigation.

In our population, oral cavity tumors had the highest percentage of patients diagnosed with local disease (stage I and II). Additionally, the largest disparity in treatment with surgery alone was in the oral cavity, likely driven by earlier stage presentation in white patients. Other studies have also shown that for cancers of the oral cavity blacks present in a later stage. Analysis of SEER data from 1973 to 2002, including 46,855 cases of oral cavity cancers, found that blacks were significantly more likely to present with more advanced stage.³⁶ Disparity in stage at diagnosis for oral cavity tumors may partially be explained by disparities in dental care. Patients referred to oral maxillofacial surgeons from a dentist office had a significantly earlier stage of disease compared to those referred from a medical office,³⁹ with numerous studies finding a lower access to routine dental care amongst blacks compared to whites.^{40, 41} With surgery being the predominant treatment of oral cavity cancers, the disparity in surgical treatment in our population was likely driven by the increased prevalence of early stage oral cavity cancers in white patients.

Compared to the oral cavity, our oropharyngeal cancer patients were more homogenous, being 82% male, with 90.1% having locally advanced disease (stage III, IVa, IVb). Treatment was primarily with chemoradiation for both races with a slightly higher number of surgically treated white patients as a result of an earlier stage at presentation driving the difference in treatment distribution for this primary site. Blacks had a significantly worse overall survival in univariate analysis with the largest disparity in outcome by race amongst patients with oropharyngeal cancer. Race was still associated with worse survival after controlling for other baseline characteristics. While we do not have data on HPV status on the full cohort in this study, based on our previous analysis⁴² we hypothesize that the significantly higher prevalence of favorable prognosis HPV positive oropharyngeal cancer in white patients may account for the observed disparity in survival this study. Our group, as well as others, have consistently observed a significantly higher prevalence of HPV positive OPSCC amongst white patients compared to blacks.²⁸⁻³¹ Recently, we analyzed 200 oropharyngeal cancer patients treated at UMGCC from 1992 to 2007, with tissue available for HPV16 testing, finding that white race was associated with a significantly higher prevalence of HPV positive OPSCC, including during each 4 year interval between 1992 to 2007.⁴² Given the magnitude of improved survival in HPV positive versus negative patients, improved outcome in whites compared to blacks in our oropharyngeal cancer subset may in part result from a higher prevalence of HPV positive cancers in our white patients.

Blacks accounted for a higher percentage of laryngeal and hypopharyngeal cancers compared to other primary sites. Increased prevalence of tobacco and alcohol consumption in our black patients may account for this, as alcohol and tobacco make up the primary risk factors for tumors at these anatomic locations. This is corroborated by SEER data reporting of age adjusted incidence rates per 100,000 patients from 2006 to 2010, which showed a higher age adjusted incidence of both laryngeal (5 vs. 3.6) and hypopharyngeal cancers (1 vs. 0.6) in blacks compared to whites, respectively (www.seer.cancer.gov). Overall survival for our hypopharyngeal cancer patients was lower than for the other sites, similar to reports in the literature.⁴³ We found no difference in overall survival between black and white patients for both laryngeal and hypopharyngeal cancers. This is in contrast to most reports where blacks fared worse for these primary sites.^{35, 44, 45} However, similar to our findings, analysis of 205 patients treated for laryngeal cancer at the Michael E DeBakey Veterans Affairs Medical center found no difference in overall survival between black and white patient, with the authors suggesting that lack of an effect of ethnicity on outcome stemmed from a uniform approach to care of a homogenous population.⁴⁶

Similar to the experience of other groups,^{27, 34} amongst our entire cohort of patients, blacks had a significantly worse overall survival including after controlling for other factors. Importantly, the overall disparity was driven largely by a more than two fold median survival difference in the subset of patients with oropharyngeal cancer. The inferior survival seen in oral cavity cancers was driven by a large number of white patients referred by dentists who were seen with stage I or II disease.

While this suggests that biological differences between black and white HNSCC patients may be contributing to the difference in outcome, our retrospective analysis cannot define the cause. Additionally, reasons for disparities in outcomes between races also involve the

interplay of patient compliance and attitude towards care, comorbidity, and other socioeconomic factors. Our study lacks data on comorbidity and compliance with treatment, both of which can affect outcomes.⁴⁷ However, in our previous analysis of 202 locally advanced HNSCC (oral cavity, oropharynx, larynx, hypopharynx) patients treated with chemoradiation at our institution between 1996 and 2006, 97% of patients completed all therapy with no difference in completion of treatment between black and white patients.²⁶ These patients represent a subset of the larger group in this report. Additionally, we were unable to quantitatively assess socioeconomic factors such as insurance status which has also been shown to effect outcomes in HNSCC.²⁰ Given that care of our HNSCC patients at UMGCC is done in a multidisciplinary fashion with consistent treatment recommendations based on stage at presentation and primary site, treatment was not included in the multivariate model to avoid overlap in variables.

Our retrospective analysis describes the experience of a single institution with a large volume and diverse group of HNSCC patients. Our analysis highlights the poor survival seen in both white and black hypopharyngeal cancer patients, and corroborates multiple other reports, where black patients have been found to have worse survival even after controlling for various other factors including smoking status and stage. While reasons for disparities in survival by race in HNSCC are complex, continued analysis should be undertaken in order to improve outcomes for all patients.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

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Figure 1.

Figure 2.

Table 1

Selected Demographic and Baseline Characteristics of the Patients (n = 1318)

Characteristic	Ethnic group			
	White	Black	Other	All patients, n=1318
Ethnicity, n, % White Black Other	NA 	NA 	NA 	869, 65.9 405, 30.7 44, 3.3
Gender, n, % Male Female	616, 70.9 253, 29.1	310, 76.5 95, 23.5	32, 72.7 12, 27.3	958, 72.7 360, 27.3
Age at diagnosis *, yrs (n=1314) Median Range	61 20-95	58 26-93	58 31-87	60 20 – 95
Smoking, n, % Yes No Unknown	573,65.9 123,14.2 173,19.9	356,87.9 23,5.7 26,6.4	25,56.8 11,25.0 8,18.2	954, 72.4 157, 11.9 207, 15.7
Alcohol, n, % Yes No Unknown	334,38.4 326,37.5 209,24.1	244,60.3 120,29.6 41,10.1	11,25.0 24,54.6 9,20.4	589,44.7 470, 35.7 259, 19.6
Smoking and Alcohol, n, % Both Smoking only Alcohol only Neither Unknown	315,36.3 217,25.0 14,1.6 108,12.4 215,24.7	241,59.5 99,24.4 2,0.5 21,5.2 42,10.4	11,25.0 12,27.3 0,0.0 11,25.0 10,22.7	567,43.0 328, 24.9 16, 1.2 140, 10.6 267, 20.3
Both, smoking and alcohol, n, % Yes No Unknown	315,36.3 339,39.0 215,24.7	241,59.5 122,30.1 42,10.4	11,25.0 23,52.3 10,22.7	567,43.0 484, 36.7 267, 20.3
Site, n, % Oral cavity Oropharynx Larynx Hypopharynx	452,52.0 240,27.6 157,18.1 20,2.3	89,22.0 125,30.9 149,36.8 42,10.4	29,65.9 8,18.2 5,11.4 2,4.5	570,43.2 373,28.3 311,23.6 64,4.9
T (tumor component), n, % 1 2 3 4 Unknown	273,31.4 227,26.1 143,16.5 203,23.4 23,2.6	69,17.0 86,21.2 104,25.7 135,33.3 11,2.7	12,27.3 14,31.8 4,9.1 14,31.8 0,0.0	354, 26.9 327, 24.8 251, 19.0 352, 26.7 34,2.6
N (node component), n, % 0 1 2 3 Unknown	426,49.0 113,13.0 266,30.6 33,3.8 31,3.6	176,43.5 37,9.1 149,36.8 31,7.6 12,3.0	22,50.0 3,6.8 15,34.1 4,9.1 0,0.0	624, 47.3 153, 11.6 430, 32.6 68, 5.2 43,3.3
M (metastasis component), n, % 0 1 Unknown	833,95.9 11,1.3 25,2.9	379,93.6 17,4.2 9,2.2	43,97.7 1,2.3 0,0.0	1255,95.2 29, 2.2 34,2.6
Year of diagnosis, n, % 2000 2001 2002 2003 2004 2005 2006	58,6.7 84,9.7 94,10.8 74,8.5 68,7.8 86,9.9 70,8.1 67,7.7	42,10.4 42,10.4 33,8.2 41,10.1 38,9.4 37,9.1 39,9.6 36,8.9	1,2.3 3,6.8 1,2.3 4,9.1 5,11.4 4,9.1 6,13.6 2,4.6	101,7.7 129, 9.8 128, 9.7 119,9.0 111,8.4 127,9.6 115,8.7 105,8.0

Characteristic	Ethnic group			
	White	Black	Other	All patients, n=1318
2007	91,10.5	31,7.7	6,13.6	128,9.7
2008	105,12.1	35,8.6	5,11.4	145, 11.0
2009	72,8.3	31,7.7	7,15.9	110,8.4
2010				
Stage, n, %	204,23.5	51,12.6	10,22.7	265,20.1
I	109,12.5	41,10.1	6,13.6	156, 11.8
II	116,13.4	59,14.6	2,4.6	177, 13.4
III	373,42.9	196,48.4	22, 50.0	591,44.8
IVa	37,4.3	33,8.2	3,6.8	73,5.5
IVb	10,1.2	17,4.2	1,2.3	28,2.1
IVc	20,2.3	8,2.0	0,0.0	28,2.1
Unknown				
Treatment	187,21.5	140,34.6	7,15.9	334,25.3
Chemo Radiotherapy	66,7.6	79,19.5	4,9.1	149,11.3
Radiotherapy	1,0.1	7,1.7	0,0.0	8,0.6
Chemotherapy, n, %	400,46.0	84,20.7	20,45.5	504,38.2
Surgery	89,10.2	50,12.4	5,11.4	144,10.9
Radiotherapy&Surgery	62,7.1	17,4.2	5,11.4	84,6.4
Chemoradiotherapy&Surgery	4,0.5	4,1.0	0,0.0	8,0.6
Chemotherapy& Surgery	60,6.9	24,5.9	3,6.8	87,6.6
Unknown				
Survival status, n, %	467,53.7	157,38.8	26,59.1	650, 49.3
Alive	402,46.3	248,61.2	18,40.9	668, 50.7
Dead				

* patients (523, 1415, 1607, 1630) do not have date of birth recorded

Table 2

Selected Demographic and Baseline Characteristics of the Patients (White and Black patients only, n=1274)*

Parameter	White (n=869) n, %	Black (n=405) n, %	p-value [†]
Gender(n=1274), n, % Male Female	616,70.9 253,29.1	310,76.5 95,23.5	0.03
Age at diagnosis [‡] , yrs (n=1271) N Median Range	868 61 20-95	403 58 26-93	0.04
Smoking (n= 1075), n,% Yes No	573,82.3 123,17.7	356,93.9 23,6.1	< 0.0001
Alcohol (n= 1024), n,% Yes No	334,50.6 326,49.4	244,67.0 120,33.0	< 0.0001
Smoking and Alcohol (n=1017), n, % Both Smoking only Alcohol only Neither	315,48.2 217,33.2 14,2.1 108,16.5	241,66.4 99,27.3 2,0.5 21,5.8	< 0.0001
Both, smoking and alcohol (n=1017), n, % Yes No	315,48.2 339,51.8	241,66.4 122,33.6	< 0.0001
Site (n= 1274), n,% Oral cavity Oropharynx Larynx Hypopharynx	452,52.0 240,27.6 157,18.1 20,2.3	89,22.0 125,30.9 149,36.8 42,10.4	< 0.0001
T (tumor component) (n=1240), n, % 1 2 3 4	273,32.3 227,26.8 143,16.9 203,24.0	69,17.5 86,21.8 104,26.4 135,34.3	< 0.0001
N (node component)(n=1231), n, % 0 1 2 3	426,50.8 113,13.5 266,31.7 33,3.9	176,44.8 37,9.4 149,37.9 31,7.9	< 0.001
M (metastasis component) (n=1240), n, % 0 1	833,98.7 11,1.3	379,95.7 17,4.3	0.001
Year of diagnosis (n=1274), n, % 2000 2001 2002 2003 2004 2005 2006 2007 2008 2009 2010	58,6.7 84,9.7 94,10.8 74,8.5 68,7.8 86,9.9 70,8.1 67,7.7 91,10.5 105,12.1 72,8.3	42,10.4 42,10.4 33,8.2 41,10.1 38,9.4 37,9.1 39,9.6 36,8.9 31,7.7 35,8.6 31,7.7	0.12
Stage (n=1246),n,% I and II III, IVa and IVb IVc	313,36.9 526,62.0 10,1.2	92,23.2 288,72.5 17,4.3	< 0.0001
Treatment (n=1190), n, %	187,23.1	140,36.8	< 0.0001

Parameter	White (n=869) n, %	Black (n=405) n, %	p-value [†]
Chemo Radiotherapy	66,8.2	79,20.7	
Radiotherapy	1,0.1	7,1.8	
Chemotherapy	400,49.4	84,22.1	
Surgery	89,11.0	50,13.1	
Radiotherapy&Surgery	62,7.7	17,4.5	
Chemoradiotherapy&Surgery	4,0.5	4,1.1	
Chemotherapy&Surgery			

Fisher's and Fisher-Freeman-Halton's tests for categorical variables and the t-test for continuous variables.

* patients with unknown status of a characteristic were excluded from the corresponding and relevant statistical test.

[†] p-values were calculated with the use of two-sided exact or with Monte Carlo simulations

[‡] The following four patients (523, 1415, 1607, 1630) do not have date of birth recorded. Also, 1D=1607 is not present in this table due to race being recorded as 'other'.

Table 3

Selected Demographic and Baseline Characteristics of the Patients by Primary Site (n = 1318)*

Parameter	Tumor Site				
	Oral Cavity (n=570)	Oropharynx (n=373)	Larynx (n=311)	Hypopharynx (n=64)	p-value [†]
Ethnicity (n=1318), n, %	452,79.3	240,64.3	157,50.5	20,31.2	< 0.0001
White	89,15.6	125,33.5	149,47.9	42,65.6	
Black	29,5.1	8,2.1	5,1.6	2,3.1	
Other					
Gender(n=1318), n, %	352,61.8	306,82.0	241,77.5	59,92.2	< 0.0001
Male	218,38.2	67,18.0	70,22.5	5,7.8	
Female					
Age at diagnosis [‡] , yrs (n=1314)	569	373	308	64	< 0.0001
N	64	57	62	57	
Median	20,95	31,88	24,90	43,89	
Range					
Smoking (n=1111),n, %	323,77.5	294,84.2	279,98.6	58,93.6	< 0.0001
Yes	94,22.5	55,15.8	4,1.4	4,6.4	
No					
Alcohol (n=1059), n, %	173,44.5	219,63.8	152,56.5	45,77.6	< 0.0001
Yes	216,55.5	124,36.2	117,43.5	13,22.4	
No					
Smoking and alcohol (n=1051), n, %	164,42.7	208,61.0	151,56.3	44,75.9	< 0.0001
Both	127,33.1	78,22.9	113,42.2	10,17.2	
Smoking only	5,1.3	10,2.9	0,0.0	1,1.7	
Drinking only	88,22.9	45,13.2	4,1.5	3,5.2	
Neither					
Both, smoking and alcohol (n=1051), n, %	164,42.7	208,61.0	151,56.3	44,75.9	< 0.0001
Yes	220,57.3	133,39.0	117,43.7	14,24.1	
No					
T (tumor component) (n=1284), n, %	228,40.6	53,14.8	68,22.7	5,7.9	< 0.0001
1	146,26.0	95,26.5	70,23.3	16,25.4	
2	27,4.8	119,33.2	82,27.3	23,36.5	
3	161,28.6	92,25.6	80,26.7	19,30.2	
4					
N (node component) (n=1275), n, %	355,63.7	68,19.0	186,62.4	15,24.2	< 0.0001
0	72,12.9	40,11.2	33,11.1	8,12.9	
1	125,22.4	208,58.1	69,23.2	28,45.2	
2	5,0.9	42,11.7	10,3.4	11,17.7	
3					
M (metastasis component) (n=1284), n, %	555,99.5	351,96.4	289,96.3	60,96.8	0.004
0	3,0.5	13,3.6	11,3.7	2,3.2	
1					
Year of diagnosis (n=1318), n, %	36,6.3	27,7.2	33,10.6	5,7.8	0.047
2000	56,9.8	40,10.7	27,8.7	6,9.4	
2001	53,9.3	37,9.9	33,10.6	5,7.8	
2002	46,8.1	44,11.8	24,7.7	5,7.8	
2003	48,8.4	30,8.0	29,9.3	4,6.2	
2004	59,10.4	32,8.6	27,8.7	9,14.1	
2005	44,7.7	40,10.7	25,8.0	6,9.4	
2006	41,7.2	29,7.8	31,10.0	4,6.2	
2007	62,10.9	23,6.2	30,9.7	13,20.3	
2008	65,11.4	44,11.8	35,11.2	1,1.6	
2009	60,10.5	27,7.2	17,5.5	6,9.4	
2010					
Stage (n=1290), n, %	280,49.7	23,6.3	113,37.7	5,7.9	< 0.0001
I and II	281,49.9	328,90.1	176,58.7	56,88.9	
III, IVa and IVb	2,0.4	13,3.6	11,3.7	2,3.2	
IVc					

Fisher's and Fisher-Freeman-Halton's tests for categorical variables and the GLM model was used for continuous variables.

* patients with unknown status of a characteristic were excluded from the corresponding and relevant statistical test.

[†] p-values were calculated with the use of two-sided exact or with Monte Carlo simulations.

[‡] four patients (523, 1415, 1607, 1630) do not have date of birth record.

Table 4

Selected Estimated Parameters of the Overall Survival (OS)*

Site	Ethnicity	N	Median, the 95%CI, yrs
All	White	869	4.8 (4.3,5.7)
	Black	405	2.5 (2.0,3.2)
	Other	44	7.7 (1.9, [†])
Oropharynx	White	240	4.9(3.7,8.1)
	Black	125	2.1 (1.5,2.9)
Oral Cavity	White	452	5.7 (4.7,7.6)
	Black	89	3.2(1.8,5.7)
Larynx	White	157	3.3 (2.3,4.5)
	Black	149	3.1 (2.3,4.9)
Hypopharynx	White	20	1.3 (0.9,3.5)
	Black	42	1.5(1.2,2.8)

* OS is defined from the date of diagnosis till the date of death from any cause or censored at the date last known alive.

[†] upper limit of the 95% CI has not been reached yet.

Table 5Overall Survival*: Results of the Multivariable Cox Regression Model All Patients (N=1001)[†]

	n	Hazard Ratio(HR) (the 95% CI)	P-value
Patients characteristics			
Ethnicity	646	1.0	0.05
White	355	1.2(1.0,1.5)	
Black			
Gender	244	1.0	0.28
Female	757	1.1 (0.9,1.4)	
Male			
Age at diagnosis, yrs	502	1.0	< 0.0001
≤59 [‡]	499	1.5(1.2,1.7)	
>59			
Both, smoking and drinking	456	1.0	< 0.0001
No	545	1.6(1.3,1.9)	
Yes			
Site	331	1.0	0.02
Oropharynx	360	1.1 (0.9,1.4)	
Oral cavity	255	1.2 (0.9,1.5)	
Larynx	55	1.8 (1.2,2.5)	
Hypopharynx			
Stage	273	1.0	< 0.0001
I and II	702	2.1 (1.7,2.6)	
III, IVa and IVb	26	6.8(4.2,11.0)	
IVc			

* OS is defined from the date of diagnosis till the date of death from any cause or censored at the date last known alive.

[†] HR=1.0 is a reference category.

[‡] age was categorized around median of 59 yrs.

Table 6

Overall Survival*: Results of the Multivariable Cox Regression Model for Patients with Cancer of Oropharynx (n=331)

Patients characteristics	N	Hazard Ratio(HR) (95%CI)	P-value
Ethnicity	218	1.0	0.002
White	113	1.6 (1.2,2.2)	
Black			
Gender	57	1.0	0.11
Female	274	0.7 (0.5,1.1)	
Male			
Age at diagnosis, yrs	158	1.0	0.34
≤56 [†]	173	1.2 (0.9,1.6)	
>56			
Both, smoking and drinking	128	1.0	< 0.0001
No	203	2.5 (1.7,3.6)	
Yes			
Stage	17	1.0	< 0.0001
I and II	302	1.2 (0.6,2.4)	
III, IVa, and IVb	12	6.9 (2.8,17.1)	
IVc			

* OS is defined from the date of diagnosis till the date of death or censored at the date last known alive

[†] median age was 56 yrs.