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Disparities in Optimal Treatment of Oral and Pharyngeal Cancer by Ethnicity and Smoking Status

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Abstract

Oral and Pharyngeal Cancer (OPC) is a deadly cancer with complex treatment plans and outcomes. In practice, surgery followed by radiation or chemotherapy is considered the "optimal treatment" associated with better OPC survival. However, not all OPC patients receive the optimal treatment. Prior research has documented that survival varies by smoking status and ethno-racial groups, but little is known about the relationship between a patient's smoking status, ethnicity, and the choices they make about cancer treatment post diagnosis. To shed light on this under-studied issue, data from the Florida Cancer Data System were analyzed. A logit model was built with the response variable treatment pattern arranged into three levels: surgery only (reference), surgery followed by radiation or chemotherapy (optimal treatment), and other treatment types consisting of all other variations of standard or alternative treatment regimens. The predictors included smoking status, race-ethnicity, smoking by race-ethnicity interaction, health insurance, age at diagnosis, sex, and marital status. The model revealed that optimal treatment varies by insurance status, and that those with a history of smoking and those diagnosed at later stages of the disease have lower odds of receiving optimal treatment. The most notable result was that the odds of optimal treatment for non-Hispanic Whites (OR=1.51, $p \leq 0.01$) and non-Hispanic Blacks (ORs=1.42-2.01, $p \leq 0.001$) were significantly higher than the odds of optimal treatment for Hispanics. One significant smoking by race-ethnicity interaction was found between non-Hispanic Blacks and current smoking status, making non-Hispanic Blacks who currently smoke less likely to receive optimal treatment than NHBs who do not smoke. These results reveal the need for more research on optimal treatment and OPC survival that control for comorbidities and socioeconomic status in addition to the control variables used in this study.

Keywords: health disparities, oral and pharyngeal cancer, treatment, survival

Introduction

Oral and Pharyngeal Cancer (OPC) is a deadly cancer with one of the lowest 5 year survival rates compared to other cancers with a similar prevalence rate (Saman, 2012). In addition to its poor survival outcomes, OPC has a high economic and psychosocial disease burden, making it a growing concern for Florida physicians, dentists, and patients (Florida Department of Health,

2016). Despite its high burden, OPC is not often a priority in research nationwide. The most recent data on OPC rates is from the CDC's Mortality and Morbidity Weekly Report, which shows OPC rates declining for some histological sites, but steadily increasing for others (CDC, 2020). More studies show that the rising and falling of rates nationwide can be explained by the success (or lack of success) of programs and legislation aimed at curbing tobacco use (Logan, 2014). Looking beyond the nationwide rates and at Florida data specifically, OPC incidence rates have been steadily climbing, with the greatest uptick occurring among Black males (CDC, 2016).

This trend alone is enough to make OPC a research focus, but there is a plethora of other characteristics that make it worthy of study. OPC is tied to systemic challenges that manifest in mortality and incidence disparities. OPC is primarily diagnosed by dentists in outpatient settings, leaving rural-dwelling individuals and those without dental insurance at a greater risk of their OPC going undetected (Logan, 2014). One of the main risk factors for OPC development is smoking, setting up ethnic groups that are known to smoke more than others to have higher incidence rates (Saman, 2012; Megwalu & Ma, 2017). OPC is also tied to low socioeconomic status and poor health literacy (Saman, 2012; Morse & Kerr, 2006). In addition to disparities in incidence, there are also known mortality disparities for OPC (Saman, 2012). Non-Hispanic White (NHW) individuals generally have better survival rates than non-Hispanic Black (NHB) individuals, but differences in survival for Hispanics compared to NHBs and NHWs is largely unknown (Morse & Kerr, 2006; Megwalu & Ma, 2017).

These disparities in survival rates are well documented up to 2016, but little is known about how they began and what contributes to their continuation in the present (Morse & Kerr, 2006). The majority of research on OPC is currently focused on screening techniques, early detection, and health literacy's impact on OPC outcomes (Guo, Logan, Marks, & Shenkman, 2015). Absent from these analyses are studies looking at optimal treatment of OPC, which greatly impacts survival. In practice, the optimal treatment for OPC cancers consists of tumor resection surgery used in tandem with chemotherapy or radiation (O'Connell et al., 2013). This treatment pattern is shown to be the most reliable in treating a majority of oral and pharyngeal cancers as well as other cancers of the head and neck (O'Connell et al., 2013). It is also the treatment course most cited for its improvement of OPC survival outcomes (O'Connell et al., 2013).

Despite the consensus both in literature and practice on the optimal treatment for OPC, almost no research has attempted to understand the distribution of treatment course decisions post-diagnosis. Considering that OPC survival rates are known to vary by socially and economically vulnerable groups and optimal treatment is hailed as a way of improving survival outcomes, it is warranted to examine if optimal treatment rates vary by demographic. This study is based on the hypothesis that optimal treatment disparities exist, and these disparities can explain the variability in survival outcomes for OPC.

Methods

Data Source

This study was approved by the University of Florida Institutional Review Board. For the purposes of this analysis, Florida presents itself as an excellent source of data to study optimal treatment of OPC. Florida is a socioeconomically and ethnically diverse state that is home to an unusually high incidence rate of OPC. Data for this analysis were acquired from the Florida Cancer Data System (FCDS), a statewide cancer registry supported by the Florida Department of Health and the Centers for Disease Control. All ambulatory surgery centers, hospitals, pathology laboratories, radiation therapy centers, and dermatopathologists' offices are required by Florida statute to report malignant cancers to the FCDS, with the exception of some skin cancers.

Selection and Definition of Variables

Florida residents over the age of eighteen who had a diagnosis of OPC in the FCDS were included in the analysis. Due to diagnostic procedure and histological differences between types of OPC cancers, cancer patient data were grouped into two categories by their ICD-0-3 site codes: those with oral cancer of the mouth floor, palate, and tongue, and those with pharyngeal cancer of the hypopharynx, oropharynx, tonsil, and the base of the tongue (NCI, 2020a). The treatment pattern used by each patient was included, indicated by surgery only (reference), surgery and radiation only or surgery and chemotherapy only (the optimal treatment), and other, defined as any other variation or sequence of alternative or traditional treatment. Ethnicity was defined as non-Hispanic White (NHW), non-Hispanic Black (NHB) or Hispanic. Smoking status was included as another variable of interest and broken down into never, current, or former smoker. Stage at diagnosis was included as a control variable, classified by SEER guidelines as either stage one, two, three, or four (NCI, 2020b). Age, sex (male or female), marital status

(married or unmarried), and source of insurance (uninsured, private insurance, Medicare, Medicaid, or other) were also included as control variables.

Data Analysis

Frequency tables were generated to understand the demographic characteristics of the patients included in the analysis. The odds of a patient receiving optimal treatment (surgery used in addition to chemotherapy or radiation) were assessed as the outcome of interest in logistic regression models. Two, separate baseline category logistic regression models were fitted for the oral cancer and pharyngeal cancer groups. In each model, treatment pattern was fitted as the categorical response variable and ethnicity, smoking status, stage at diagnosis, age, sex, marital status, insurance status and race-ethnicity by smoking status interaction were included as predictors. All effects were estimated as odds rations (ORs) with 95% confidence intervals (CIs). All analyses were completed with R 3.4.4.

Results

Odds of Optimal Treatment of Oral Cancer

Coefficients taken from the baseline category logistic regression model of the oral cancer group were used to generate odds ratios and 95% confidence intervals for the exponentiated coefficients.

odds of optimal treatment versus surgery only.

For the oral cancer group, NHBs were 41.6% more likely to receive optimal treatment over surgery only than Hispanics. NHWs were 50.8% more likely to receive optimal treatment over surgery. In this group, former and current smoking status were not associated with optimal treatment versus surgery only, but stage at diagnosis was. The odds of optimal treatment were highest when an individual was diagnosed at stage one (the reference group) but decreased if the cancer was diagnosed one stage later. Those diagnosed at stage two had an odds of optimal treatment 79.5% lower than the odds of optimal treatment for those diagnosed at stage one. The odds were even lower for those diagnosed at stage two, making them 82.2% less likely to receive optimal treatment over surgery only than those diagnosed at stage one. The odds of optimal treatment increased slightly between diagnoses at stage three and four, making those diagnosed at stage four 55.7% less likely to receive optimal treatment than those diagnosed at stage one. No notable associations between insurance status and optimal treatment over surgery were found in this group.

Table 1. Odds of Optimal Treatment vs. Surgery for Oral Cancer Patients

Factor	Level	Odds Ratio	Confidence Interval of Odds
		e^{β}	95% CI on e^{β}
Ethnicity	Hispanic (Reference)	1.000	
	Non-Hispanic Black	1.416**	(1.002. 1.980)
	Non-Hispanic White	1.508**	(1.125, 2.020)
Smoking Status	Never Smoker (Reference)	1.000	
	Current Smoker	1.362	(0.915, 2.028)
	Former Smoker	0.796	(0.514, 1.230)
Stage at Diagnosis	Stage 1 (Reference)	1.000	
	Stage 2	0.205***	(0.186, 0.225)
	Stage 3	0.178***	(0.151, 0.210)
	Stage 4	0.443***	(0.390, 0.503)
Sex	Female (Reference)	1.000	
	Male	1.001	(0.918, 1.092)
Age at Diagnosis	Age (Continuous)	1.009***	(1.005, 1.012)
Marital Status	Married (Reference)	1.000	
	Unmarried	0.932	(0.855, 1.016)
Insurance Status	Uninsured (Reference)	1.000	
	Private	0.843	(0.705, 1.063)
	Medicaid	0.840	(0.643, 1.096)
	Medicare	0.978	(0.792, 1.209)
	Other	0.811	(0.651, 1.010)

Note. ***p≤0.001, **p≤0.01, *p≤0.05.

odds of optimal treatment versus other treatment.

Comparing the odds of optimal treatment versus other treatment, NHBs were close to two times more likely to receive optimal treatment over other treatment than Hispanics. The odds for NHWs did not significantly differ from the odds of optimal treatment for Hispanics. Unlike the odds of optimal treatment versus surgery only, the odds of optimal treatment over other treatment was strongly associated with smoking status. Current smokers were 75.3% less likely and former smokers were 49.6% less likely to receive optimal treatment over other treatment than nonsmokers.

There was no difference in the odds of optimal treatment over other treatment between those diagnosed at stage one and two, but those diagnosed at stages three and four were each 45% less likely to receive optimal treatment over other treatment. Males were 18.8% less likely to receive

optimal treatment over other treatment than females, and those who were unmarried were 39.7% more likely to receive optimal treatment than those who were married. Private insurance (OR=1.796, p≤0.001), Medicare (OR=2.113, p≤0.001), and other insurance (OR=1.759, p≤0.001) were all associated with an increase in the odds of optimal treatment over other treatment compared to no insurance. There was no significant difference in the odds of optimal treatment versus other treatment rates between those who were uninsured and those who were on Medicaid.

Table 2. Odds of Optimal Treatment vs. Other Treatment for Oral Cancer Patients

Factor	Level	Odds Ratio	Confidence Interval of Odds
		e^{β}	95% CI on e^{β}
Ethnicity	Hispanic (Reference)	1.000	
	Non-Hispanic Black	2.089***	(1.329, 3.286)
	Non-Hispanic White	1.256	(0.846, 1.864)
Smoking Status	Never Smoker (Reference)	1.000	
	Current Smoker	0.247***	(0.156, 0.392)
	Former Smoker	0.504***	(0.307, 0.826)
Stage at Diagnosis	Stage 1 (Reference)	1.000	
	Stage 2	1.075	(0.954, 1.211)
	Stage 3	0.553***	(0.469, 0.650)
	Stage 4	0.552***	(0.466, 0.653)
Sex	Female (Reference)	1.000	
	Male	0.812***	(0.709, 0.930)
Age at Diagnosis	Age (Continuous)	0.970***	(0.964, 0.976)
Marital Status	Married (Reference)	1.000	
	Unmarried	1.397**	(1.225, 1.594)
Insurance Status	Uninsured (Reference)	1.000	
	Private	1.796***	(1.434, 2.250)
	Medicaid	0.868	(0.656, 1.149)
	Medicare	2.113***	(1.669, 2.677)
	Other	1.759***	(1.361, 2.275)

Note. ***p≤0.001, **p≤0.01, *p≤0.05.

Odds of Optimal Treatment of Pharyngeal Cancer

Coefficients taken from the baseline category logistic regression model of the pharyngeal cancer group were used to generate odds ratios and 95% confidence intervals for the exponentiated coefficients.

odds of optimal treatment versus surgery only.

There was no difference in the odds of optimal treatment versus surgery only between NHWs and Hispanics. NHBs, however, were 69.8% more likely to receive optimal treatment over surgery only than Hispanics. One significant interaction was found between race-ethnicity and smoking status comparing optimal treatment versus surgery only, making NHB individuals who were current smokers 41.9% less likely to receive optimal treatment over surgery. No associations were found with smoking status alone. Stage at diagnosis in the pharyngeal group was also associated with a lower likelihood of optimal treatment over surgery only. Those diagnosed at stages two and three were 74% less likely to receive optimal treatment over surgery only than those diagnosed at stage one. Those diagnosed at stage four were 47.7% less likely to receive optimal treatment. Males in this group were 20.4% less likely to receive optimal treatment over surgery than females. The only insurance level that was associated with the odds of optimal treatment over surgery was Medicaid. Those on Medicaid were 34.8% less likely to receive optimal treatment over surgery only than the uninsured.

Table 3. Odds of Optimal Treatment vs. Surgery for Pharyngeal Cancer Patients

Factor	Level	Odds Ratio	Confidence Interval of Odds
		e^{β}	95% CI on e^{β}
Ethnicity	Hispanic (Reference)	1.000	
	Non-Hispanic Black	1.698***	(1.022, 3.344)
	NHB:Current Smoker	0.581***	(0.357, 0.942)
	Non-Hispanic White	1.241	(0.698, 2.208)
Smoking Status	Never Smoker (Reference)	1.000	
	Current Smoker	1.541	(0.805, 2.905)
	Former Smoker	0.887	(0.454, 1.736)
Stage at Diagnosis	Stage 1 (Reference)	1.000	
	Stage 2	0.263***	(0.229, 0.333)
	Stage 3	0.258***	(0.204, 0.325)
	Stage 4	0.523***	(0.436, 0.627)
Gender	Female (Reference)	1.000	
	Male	0.796***	(0.701, 0.903)
Age at Diagnosis	Age (Continuous)	1.021	(0.594, 1.032)
Marital Status	Married (Reference)	1.000	
	Unmarried	0.973	(0.927, 1.028)
Insurance Status	Uninsured (Reference)	1.000	
	Private	0.782	(0.594, 1.032)
	Medicaid	0.652**	(0.459, 0.927)
	Medicare	0.878	(0.659, 1.170)
	Other	0.765	(0.571, 1.022)

Note. ***p≤0.001, **p≤0.01, *p≤0.05.

odds of optimal treatment versus other treatment.

Comparing the odds of optimal treatment versus other treatment for the pharyngeal group, there was no significant difference between the rates of treatment between NHBs, NHWs, and Hispanics. Current smokers were 45.7% less likely to receive optimal treatment over other treatment than those who had never smoked. For stage at diagnosis, those diagnosed at stage two were 15.2% more likely to receive optimal treatment over other treatment than those diagnosed at stage one. Those diagnosed at stage three, however, were 32.3% less likely to receive optimal treatment. Those who were unmarried were 28.4% less likely to receive optimal treatment over other treatment than those who were married. The odds of optimal treatment for those on private insurance (OR=1.682, p≤0.01), Medicare (OR=1.809, p≤0.001), and other insurance (OR=1.900,

p≤0.05) were higher than the odds of optimal treatment for the uninsured. There was no significant difference in the odds of optimal treatment between those on Medicaid and the uninsured.

Table 4. Odds of Optimal Treatment vs. Other Treatment for Pharyngeal Cancer Patients

Factor	Level	Odds Ratio	Confidence Interval of Odds
		e^{β}	95% CI on e^{β}
Ethnicity	Hispanic (Reference)	1.000	
	Non-Hispanic Black	0.735	(0.464, 1.165)
	Non-Hispanic White	1.517	(1.041, 2.210)
Smoking Status	Never Smoker (Reference)	1.000	
	Current Smoker	0.543**	(0.356, 0.827)
	Former Smoker	1.066	(0.695, 1.635)
Stage at Diagnosis	Stage 1 (Reference)	1.000	
	Stage 2	1.152***	(1.035, 1.282)
	Stage 3	0.677***	(0.572, 0.801)
	Stage 4	1.035	(0.879, 1.219)
Gender	Female (Reference)	1.000	
	Male	1.027	(0.867, 1.216)
Age at Diagnosis	Age (Continuous)	0.971***	(0.964, 0.979)
Marital Status	Married (Reference)	1.000	
	Unmarried	0.716***	(0.627, 0.816)
Insurance Status	Uninsured (Reference)	1.000	
	Private	1.682**	(1.387, 2.039)
	Medicaid	1.109	(0.893, 1.377)
	Medicare	1.809***	(1.482, 2.207)
	Other	1.900*	(1.489, 2.197)

Note. ***p≤0.001, **p≤0.01, *p≤0.05.

Discussion

In this analysis, we found Hispanics were less likely to receive optimal treatment for oral and pharyngeal cancers compared to non-Hispanics, and NHBs were often more likely to receive optimal treatment than NHWs. NHBs with pharyngeal cancer, though more likely to receive optimal treatment over Hispanics, were less likely to receive optimal treatment if they were current smokers. In most comparisons for both the oral and pharyngeal models, the odds of optimal treatment for those on Medicaid were not significantly different from the odds for those

who were uninsured. In the one comparison in which Medicaid was significantly associated with treatment pattern, it corresponded with lower odds of optimal treatment than the odds for the uninsured.

Considering that the odds of optimal treatment for Hispanics were lower than the odds of optimal treatment for both NHWs and NHBs in several comparisons, it would follow that Hispanics would have poorer survival outcomes than NHBs and NHWs. However, making this connection is not currently possible due to a lack of reliable data differentiating OPC survival rates for Hispanics from other ethno-racial groups (Morse & Kerr, 2006; Megwalu & Ma, 2017). In several comparisons, NHBs had higher odds of optimal treatment than both NHWs and Hispanics, even though NHBs are known to generally have poorer OPC outcomes than NHWs (Megwalu & Ma, 2017). This suggests that there are other risk factors that caused the observed ethno-racial differences in treatment options, possibly explaining why the distribution of treatment choices does not agree with the distribution of OPC outcomes.

In our multivariable analysis, many risk factors were included as control variables, including age, gender, smoking status, marital status, stage of diagnosis, and insurance. One variable lacking from the controls in this study, however, is comorbid conditions, such as diabetes or cardiovascular diseases. Comorbid conditions are important considerations when making decisions on the course of treatment for any cancer. Patients with more severe comorbid conditions are often less likely to undergo the optimal treatment, which includes more extensive treatment rather than just one therapy alone. Another important factor that was unavailable in the FCDS data is income. There is a rich literature on how income impacts cancer treatment decisions and cancer prognosis. Insurance status was available in FCDS data, which served as a surrogate for income in our analysis. Nonetheless, one limitation of our study is FCDS's lack of access to additional risk factors for analysis.

Conclusion

Overall, our results have highlighted the importance of conducting more research to better understand the risk factors behind the ethno-racial disparities in OPC treatment choices. Gaining a comprehensive view of all potential risk factors is critically important for designing culturally appropriate interventions that aim to minimize the ethno-racial disparities in OPC treatment and survival. In recent years, rapid adoption of electronic health records (EHRs) systems has made large-scale, longitudinal clinical data available for research. These EHRs usually contain a

comprehensive list of important risk factors for cancer outcomes, such as disease diagnosis, health care utilization, social determinants of health, and more. Future research could leverage the huge amount of clinical data in EHRs to better understand the ethno-racial disparities in OPC treatment choices.

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