Academic Affiliation and Surgical Volume Predict Survival in Head and Neck Cancer Patients Receiving Surgery

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Objective: To determine whether the academic affiliation or surgical volume affects the overall survival (OS) of human papillomavirus (HPV)–negative head and neck squamous cell carcinoma (HNSCC) patients receiving surgery.

Methods: A retrospective study of 39 North Carolina Medical Centers was conducted. Treatment centers were classified as academic hospitals, community cancer centers, or community hospitals and were divided into thirds by volume. The primary outcome was 5-year OS. Hazard ratios (HR) were determined using Cox proportional hazard models, adjusting for demographics, tumor site, stage, insurance status, tobacco use, alcohol use, stage, chemotherapy, and radiation therapy. Patients were also stratified by stage (early stage and advanced stage).

Results: Patients treated at community cancer centers had significantly better 5-year OS (HR 0.68, 95% confidence interval [CI] = 0.48–0.98), and patients treated at academic hospitals trended toward better 5-year OS (HR 0.72, 95% CI = 0.50–1.04) compared to patients treated at community hospitals. The effect for academic affiliation on survival was more pronounced for patients with advanced stage cancer at diagnosis (HR 0.60, 95% CI = 0.37–0.95). There were no significant survival differences among early stage patients by treatment center type. Top-third (HR = 0.64, 95% CI = 0.42–0.96) centers by surgical volume had significantly better 5-year OS, and middle-third (HR = 0.71, 95% CI = 0.51–1.03) centers by volume trended toward better 5-year OS when compared to the bottom-third centers by volume.

Conclusion: Patients treated at academic hospitals, community cancer centers, and hospitals in the top third by case volume have favorable survival for HPV-negative HNSCC. The effect for academic hospitals is most pronounced among advanced stage patients.

Key Words: academic medicine, academic medical center cancer center, head and neck cancer, head and neck squameous cell carcinoma, private hospital, survival, stage.

Level of Evidence: 4

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INTRODUCTION

With an annual incidence of over 550 thousand cases and 300 thousand deaths, head and neck squamous cell carcinoma (HNSCC) represents the sixth leading malignancy worldwide, and human papillomavirus (HPV)-negative HNSCC patients tend to have poor survival outcomes compared to many other common malignancies.[1–3] Demographic, clinical, and socioeconomic exposures have been well researched in head and neck cancer and are known to affect survival outcomes.[4,5] A variable that has received proportionally less attention in literature is the surgical treatment center. Surgery for HNSCC patients is performed at both academic- and community-based medical centers with a wide range of HNSCC surgical volumes, and these characteristics may affect survival outcomes.

The impact of treatment center volume on patient outcomes has been studied in several other malignancies.[6–9] Several studies have also investigated treatment center volume and patient outcomes in head and neck cancer. One study performed a comparative analysis of head and neck oncologic surgery outcomes across various academic centers and found that academic centers with higher case volumes had lower rates of complications.[10] However, community medical centers were not included in the analysis of that study. Another study demonstrated that high-volume academic centers had lower intensive care units stays but no differences in mortality in a geriatric population treated for head and neck cancer.[11] Further studies demonstrated that patients with nasopharyngeal carcinoma had better overall survival when treated at higher volume centers.[12] Overall, there is growing evidence that treatment centers with

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higher surgical volumes have favorable perioperative outcomes across multiple diseases.[13–17]

There is considerably less evidence in current literature examining the impact of academic affiliation on HNSCC survival outcomes. One study found that for patients with HNSCC being treated with definitive radiotherapy, treatment at an academic facility was associated with improved overall survival even after adjusting for demographic, clinical, and socioeconomic factors.[18] A similar study demonstrated improved survival outcomes in patients who received upfront or adjuvant radiation therapy in an academic center versus a community center, despite a larger proportion of advanced stage patients in the academic centers.[19] A proposed mechanism for this association is increased access to subspecialty expertise and multidisciplinary care at academic centers. This mechanism could potentially be applied to patients with HNSCC treated surgically as well. To our knowledge, however, no studies have examined the relationship between academic affiliation and survival outcomes in a sample of HNSCC patients treated surgically with curative intent.

The aim of this study is to determine whether the academic affiliation or surgical volume of treatment centers affects overall survival for HPV-negative HNSCC patients treated surgically. We also stratified patients by stage to determine whether treatment centers differentially affect survival for early or advanced stage patients.

METHODS

Population

The patient population consisted of participants in the Carolina Head and Neck Cancer Epidemiology Study (CHANCE).[20,21] This was a statewide population-based case-control study that was conducted in North Carolina from January 2002 to February 2006. The aim was to capture the demographics, risk factors, and treatment courses of the population of head and neck cancer patients in North Carolina. Cases were identified through the North Carolina Central Cancer Registry, which includes all cancer patients treated in the state. Patients were eligible if they had been diagnosed with a first primary squamous cell carcinoma of the oral cavity, pharynx, or larynx between January 1, 2002, and February 28, 2006; were ages 20 to 80 years at diagnosis; and resided in a 46-county region in central North Carolina. Contact and cooperation rates were 98% and 82%, respectively. CHANCE patients were only included in our study if their tumor was treated with curative surgery, with or without adjuvant therapy. The institutional review board of the University of North Carolina at Chapel Hill approved this retrospective analysis.

Patient Characteristics

Demographics, income, insurance status, tobacco use, alcohol consumption, insurance status, educational attainment, and income level were assessed by trained nurse-interviewers using a structured questionnaire during an in-home visit. These were categorized in the final dataset instead of recorded as continuous variables. The income cutoffs reflect 100% ($20,000) and 250% ($50,000) of the federal poverty level (FPL) for a family of 4 at the time of data collection in 2006.[22,23] The age cutoffs are based on those commonly used in published literature. The pack-year smoking categorization was based on the minimum cutoff necessary to ensure an adequate sample distribution with sufficient numbers in each category. Alcohol use was recorded as a dichotomous variable (any vs. none) in the dataset. Tumor pathology notes were examined to determine staging by the American Joint Committee on Cancer (AJCC) seventh edition criteria. Tumors were classified by tumor (T) stage (T1–4), nodal (N) stage (N 0–3), and location of tumor (larynx, hypopharynx, oral cavity, and oropharynx). T and N staging were used to classify patients into early stage (stages I and II) and advanced stage (stages III and IV) groups. Patients with distant metastases, palliative surgery, HPV positive tumor status, and T4b disease were excluded.

Outcome

The primary outcome was 5-year overall survival. Deaths were determined through the National Death Index, linking on name, Social Security number, date of birth, sex, race, and state of residence. Deaths were identified through December 31, 2013; 5-year follow-up was available for every patient.

Treatment Center Designation

Surgical treatment centers were categorized as academic centers or community cancer centers based on National Cancer Institute (NCI) designations. Veterans Affairs (VA) hospitals affiliated with an academic institution were categorized as academic centers. At the time of the study, all academic centers in our study in North Carolina were classified as cancer centers. Hospitals without an NCI designation or academic affiliation were categorized as community hospitals. Of 39 surgical sites, there were a total of five academic centers, nine community cancer centers, and 25 community hospitals.

Surgical HNSCC volume was determined by evaluating the total volume of study patients operated on at each center. Sites were divided into thirds based on total surgical treatment volume over the study period. By tertile, the volume cutoffs were one to 16 patients for the first (mean 9.7), 18 to 41 for the second (mean 30.9), and 59 to 71 for the third (mean 65.6). CHANCE identified patients from a state-wide cancer registry without regard to treating institutions; thus, the total number of CHANCE patients treated served as a proxy for total HNSCC patients treated over that time period.

Statistical Analysis

Statistical analysis was performed using chi-square testing for categorical variables. Hazard ratios (HR) and 95% confidence intervals (CI) were calculated using Cox proportional hazards models for overall survival. We constructed three models to assess the combined and independent effects of hospital affiliation and hospital volume on overall survival. Model 1 included both hospital affiliation and hospital volume; model 2 included only hospital affiliation; and model 3 included only hospital volume. All models were adjusted for age, sex, race, tumor site, insurance status, tobacco use, alcohol use, overall stage (AJCC), chemotherapy, and radiation therapy. Pearson r was used to assess for correlation between hospital affiliation and hospital volume in the combined model. Multiplicative interaction terms were created between 1) overall stage and hospital affiliation, and 2) overall stage and hospital volume to assess for the potential role of stage as an effect measure modifier. For each model, we reported results for all patients as well as patients with either early (I to II) or advanced (III to IV) overall stage. Stratification by stage was done for clinical relevance rather than statistical indication (P value = .212 for interaction term 1,

TABLE I.
Patient Demographics, Tumor Characteristics, and Treatment Received by Hospital Type and Volume.

	Site Affiliation							Site Volume						
	Academic		Community Cancer Center		Community Hospital		*P* Value	Bottom Third		Middle Third		Top Third		*P* Value
	No.	%	No.	%	No.	%		No.	%	No.	%	No.	%	
Age category														
< 50 (n = 100)	32	24%	30	19%	38	22%	.65	26	15%	41	25%	33	25%	.098
50–65 (n = 212)	63	48%	73	47%	76	43%		78	46%	73	45%	61	47%	
65+ (n = 151)	37	28%	52	34%	62	35%		65	38%	50	30%	36	28%	
Sex														
Male (n = 328)	95	72%	110	71%	123	70%	.92	121	72%	113	69%	94	72%	.786
Female (n = 135)	37	28%	45	29%	53	30%		48	28%	51	31%	36	28%	
Race														
White (n = 337)	102	77%	108	70%	127	72%	.34	137	81%	110	67%	90	69%	.009
Black (n = 126)	30	23%	47	30%	49	28%		32	19%	54	33%	40	31%	
Education														
Less than high school (n = 162)	44	33%	53	34%	65	37%	.47	54	32%	58	35%	50	38%	.061
High school graduate (n = 127)	35	27%	38	25%	54	31%		43	25%	56	34%	28	22%	
Greater than high school (n = 174)	53	40%	64	41%	57	32%		72	43%	50	30%	52	40%	
Income														
Income > $50,000 (n = 128)	34	26%	53	34%	41	23%	.19	49	29%	40	24%	39	30%	.821
Income $20,000–$50,000 (n = 161)	49	37%	45	29%	67	38%		59	35%	58	35%	44	34%	
Income < $20,000 (n = 174)	49	37%	57	37%	68	39%		61	36%	66	40%	47	36%	
Insurance														
Private (n = 164)	44	33%	53	34%	67	38%	.88	60	36%	56	34%	48	37%	.714
Medicaid/Medicare (n = 170)	53	40%	58	37%	59	34%		61	36%	59	36%	50	38%	
None (n = 50)	15	11%	18	12%	17	10%		15	9%	19	12%	16	12%	
Other (n = 79)	20	15%	26	17%	33	19%		33	20%	30	18%	16	12%	
Smoking														
< 10 years (n = 103)	31	23%	38	25%	34	19%	.48	42	25%	33	20%	28	22%	.569
> 10 years (n = 360)	101	77%	117	75%	142	81%		127	75%	131	80%	102	78%	
Alcohol use														
None (n = 82)	29	22%	25	16%	28	16%	.32	29	17%	32	20%	21	16%	.735
Any (n = 381)	103	78%	130	84%	148	84%		140	83%	132	80%	109	84%	
Site														
Hypopharynx (n = 10)	2	2%	2	1%	6	3%	.35	4	2%	5	3%	1	1%	.399
Larynx (n = 155)	44	33%	39	25%	72	41%	.01	69	41%	60	37%	26	20%	<.001
Oral cavity (n = 226)	66	50%	89	57%	71	40%	.01	76	45%	74	45%	76	58%	.034
Oropharynx (n = 72)	20	15%	25	16%	27	15%	.97	20	12%	25	15%	27	21%	.106
T stage														
T1 (n = 171)	43	33%	59	38%	69	39%	.082*	74	44%	51	31%	46	35%	.005*
T2 (n = 148)	38	29%	51	33%	59	34%		56	33%	48	29%	44	34%	
T3 (n = 64)	19	14%	27	17%	18	10%		18	11%	24	15%	22	17%	
T4 (n = 80)	32	24%	18	12%	30	17%		21	12%	41	25%	18	14%	
N stage														
N0 (n = 287)	75	57%	95	61%	117	66%	.19	133	79%	86	52%	68	52%	<.001
N1 (n = 66)	17	13%	28	18%	21	12%		16	9%	27	16%	23	18%	
N2 (n = 101)	35	27%	30	19%	36	20%		20	12%	46	28%	35	27%	
N3 (n = 9)	5	4%	2	1%	2	1%		0	0%	5	3%	4	3%	
TNM stage														
I (n = 139)	31	23%	47	30%	61	35%	.116**	31	23%	47	30%	61	35%	<.001*
II (n = 92)	26	20%	30	19%	36	20%		26	20%	30	19%	36	20%	
III (n = 70)	16	12%	33	21%	21	12%		16	12%	33	21%	21	12%	

(Continues)

TABLE I.
Continued

	Site Affiliation							Site Volume						
	Academic		Community Cancer Center		Community Hospital		*P* Value	Bottom Third		Middle Third		Top Third		*P* Value
IVA (n = 151)	53	40%	43	28%	55	31%		53	40%	43	28%	55	31%	
IVB (n = 11)	6	5%	2	1%	3	2%		6	5%	2	1%	3	2%	
Treatment category														
Surgery only (n = 221)	55	42%	85	55%	81	46%	<.001	79	47%	74	45%	68	52%	.033
Surgery + postoperative chemoradiation (n = 69)	35	27%	16	10%	18	10%		16	9%	27	16%	26	20%	
Surgery + postoperative chemotherapy (n = 1)	1	1%	0	0%	0	0%		0	0%	1	1%	0	0%	
Surgery + postoperative radiation (n = 172)	41	31%	54	35%	77	44%		74	44%	62	38%	36	28%	
Volume category:														
Bottom third (n = 169)	10	8%	61	39%	98	56%	<.001							
Middle third (n = 164)	63	48%	23	15%	78	44%								
Top third (n =130)	59	45%	71	46%	0	0%								

**P*-value for advanced stage vs. early-stage.
TNM = tumor-node-metastasis.

TABLE II.
Multivariable Cox Regression Model for 5-Year Overall Survival Incorporating Hospital Type and Hospital Volume.

	All Patients *(n = 463)*			Early Stage (n = 231)			Advanced Stage (n = 232)		
Variables	Hazard Ratio	95% CI	*P Value*	Hazard Ratio	95% CI	*P* Value	Hazard Ratio	95% CI	*P* Value
Hospital Type (relative to community hospital)									
Community Cancer Center	0.70	0.47–1.03	.070	0.99	0.54–1.82	.987	0.63	0.37–1.07	.085
Academic	0.82	0.54–1.24	.356	1.45	0.67–3.16	.349	0.64	0.39–1.06	.081
Hospital Volume (relative to bottom third)									
Middle Third	0.71	0.49–1.03	.071	0.51	0.25–1.05	.067	0.78	0.49–1.24	.294
Top Third	0.73	0.46–1.15	.175	0.60	0.27–1.31	.199	0.80	0.44–1.45	.465
Site (relative to larynx)									
Hypopharynx	1.82	0.83–3.99	.133	NA			2.00	0.90–4.46	.091
Oral cavity	1.18	0.82–1.69	.383	1.21	0.62–2.37	.572	1.12	0.70–1.78	.646
Oropharynx	1.13	0.70–1.85	.610	2.71	1.13–6.51	.026	0.93	0.51–1.68	.800
Age	1.01	1.00–1.03	.138	1.03	1.00–1.06	.082	1.00	0.98–1.02	.942
Female sex (relative to male)	0.80	0.55–1.16	.230	0.75	0.42–1.34	.330	0.78	0.46–1.30	.331
Non-white (vs. white)	1.11	0.77–1.59	.568	1.30	0.70–2.41	.399	0.95	0.61–1.49	.832
Insurance (relative to private)									
Medicaid/Medicare	2.12	1.34–3.36	.001	1.94	0.92–4.06	.081	2.33	1.28–4.27	.006
None	2.51	1.51–4.15	.000	1.88	0.61–5.82	.275	2.80	1.53–5.13	.001
Other	2.02	1.21–3.38	.007	0.84	0.35–2.00	.687	3.55	1.82–6.94	.000
Smoking (> 10 pack-years)	1.06	0.70–1.61	.777	1.06	0.53–2.12	.870	1.00	0.58–1.71	.988
Alcohol use (Any)	1.10	0.67–1.80	.703	1.66	0.76–3.61	.203	0.81	0.41–1.58	.537
TNM stage (relative to stage I)									
Stage II	1.41	0.87–2.29	.169	1.21	0.71–2.09	.483	NA		
Stage III	1.96	1.16–3.33	.012	NA			NA		
Stage IV	2.87	1.79–4.60	.000	NA			1.47	0.92–2.35	.110*
Adjuvant radiation	1.11	0.77–1.60	.581	1.07	0.56–2.07	.831	1.04	0.63–1.71	.890
Adjuvant chemotherapy	0.92	0.58–1.48	.745	NA			1.02	0.62–1.67	.947

**P* value for stage IV vs. stage III.
TNM = tumor-node-metastasis.

TABLE III.
Multivariable Cox Regression Model for 5-Year Overall Survival Based on Hospital Type.

	All Patients (n = 463)			Early Stage (n = 231)			Advanced Stage (n = 232)		
Variables	Hazard Ratio	95% CI	*P* Value	Hazard Ratio	95% CI	*P* Value	Hazard Ratio	95% CI	*P* Value
Hospital type (relative to community hospital)									
Community cancer center	0.68	0.48–0.98	.037	0.95	0.54–1.68	.867	0.62	0.39–1.00	.048
Academic	0.72	0.50–1.04	.083	1.04	0.56–1.94	.896	0.60	0.37–0.95	.031
Site (relative to larynx)									
Hypopharynx	1.91	0.88–4.17	.103	NA			2.04	0.92–4.54	.080
Oral cavity	1.15	0.80–1.65	.447	1.29	0.67–2.50	.444	1.10	0.70–1.73	.685
Oropharynx	1.11	0.68–1.79	.680	2.57	1.07–6.16	.035	0.92	0.51–1.66	.779
Age	1.01	1.00–1.03	.132	1.03	1.00–1.06	.075	1.00	0.98–1.02	.962
Female sex (relative to male)	0.78	0.54–1.13	.186	0.69	0.39–1.24	.216	0.78	0.47–1.30	.349
Non-white (vs. white)	1.05	0.74–1.50	.769	1.17	0.64–2.13	.617	0.93	0.60–1.45	.752
Insurance (relative to private)									
Medicaid/Medicare	2.12	1.34–3.35	.001	1.92	0.93–3.97	.078	2.31	1.27–4.21	.006
None	2.55	1.54–4.22	.000	1.87	0.61–5.74	.277	2.85	1.56–5.20	.001
Other	2.01	1.20–3.37	.008	0.82	0.35–1.96	.662	3.55	1.82–6.94	.000
Smoking (> 10 pack-years)	1.05	0.70–1.58	.820	1.00	0.51–1.99	.990	1.00	0.59–1.70	.996
Alcohol use (any)	1.11	0.68–1.81	.681	1.75	0.80–3.81	.162	0.80	0.41–1.56	.519
TNM stage (relative to stage I)									
Stage II	1.40	0.86–2.27	.180	1.20	0.69–2.07	.519	NA		
Stage III	1.83	1.08–3.10	.024	NA			NA		
Stage IV	2.54	1.60–4.02	.000	NA			1.44	0.90–2.29	.129*
Adjuvant radiation	1.16	0.80–1.67	.428	1.33	0.72–2.47	.358	1.02	0.62–1.68	.926
Adjuvant chemotherapy	0.92	0.58–1.48	.743	NA			1.02	0.63–1.66	.934

**P* value for stage IV vs. stage III.
CI = confidence interval; NA = nonapplicable; TNM = tumor-node-metastasis.

P value = .618 for interaction term 2). Kaplan-Meier survival plots were constructed for both overall survival and survival by stage. Significance was set at $P < .05$. All statistical analysis was performed using STATA/IC 15.0 software (Stata Corporation, College Station, TX).

RESULTS

Population Characteristics

A total of 463 patients met inclusion criteria for the study. The average age of the cohort was 59.2 (standard deviation 10.7); patients were 71% male and 77% white. Within this population, 231 patients (50%) had stage 1 or stage 2 cancers, and 232 (50%) had stage 3 or 4. By site, 226 (49%) had oral cavity cancer; 155 (33%) had laryngeal cancer; 72 (16%) had oropharyngeal cancer; and 10 (2%) had hypopharyngeal cancer.

We first compared the demographics, behaviors, tumor characteristics, and treatments between patients who received surgery at academic centers, community cancer centers, and community hospitals. There were no significant differences in age, sex, race, education, income, insurance status, tobacco use, or alcohol use (Table I). There were also no significant differences in the presence of nodal metastases, T stage, or overall stage among patients treated at different sites. Academic and community cancer centers treated a higher proportion of oral cavity cancers than community hospitals (50% and 57% vs. 40%; *P* = .01) and a lower proportion of laryngeal cancers (33% and 25% vs. 41%; *P* = .01). Patients treated at academic centers were significantly more likely to receive chemoradiation in addition to surgery (27% for

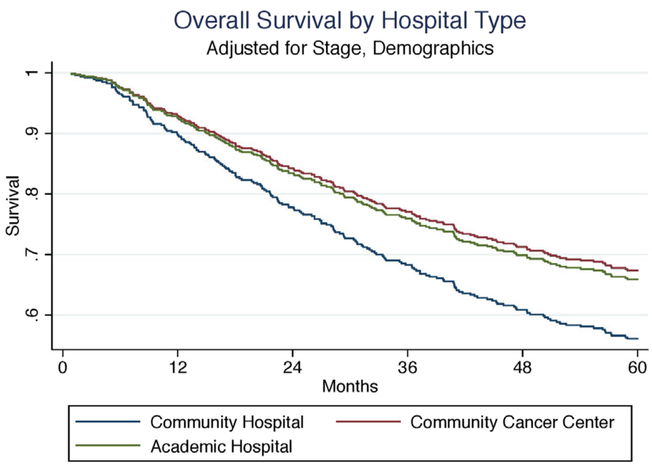

Fig. 1. Adjusted overall survival based on treatment center type using a Cox proportional hazards model.

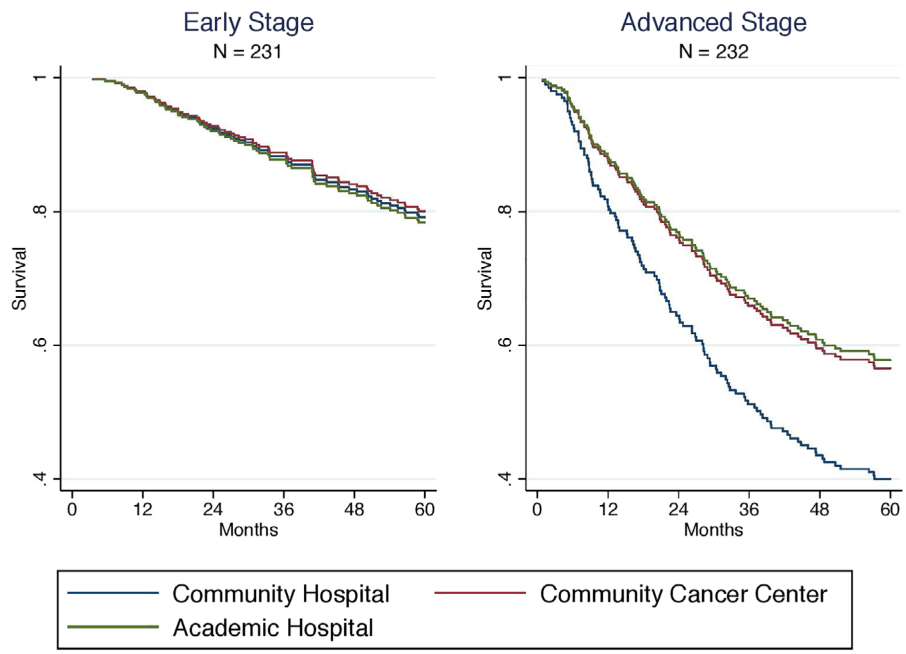

Fig. 2. Adjusted overall survival based on overall stage and treatment center using a Cox proportional hazards model.

TABLE IV.
Multivariable Cox Regression Model for 5-Year Overall Survival Based on Hospital Volume.

Variables	All Patients (n = 463)			Early Stage (n = 231)			Advanced Stage (n = 232)		
	Hazard Ratio	95% CI	*P* Value	Hazard Ratio	95% CI	*P* Value	Hazard Ratio	95% CI	*P* Value
Hospital volume (relative to bottom third)									
Middle third	0.72	0.51–1.03	.074	0.59	0.30–1.14	.116	0.76	0.49–1.19	.235
Top third	0.64	0.42–0.96	.029	0.74	0.39–1.40	.348	0.63	0.37–1.07	.086
Site (relative to larynx)									
Hypopharynx	1.75	0.80–3.85	.161	NA			1.93	0.86–4.33	.113
Oral cavity	1.15	0.80–1.66	.441	1.28	0.66–2.46	.467	1.14	0.72–1.82	.576
Oropharynx	1.12	0.69–1.81	.654	2.66	1.11–6.39	.029	0.94	0.52–1.70	.834
Age	1.01	0.99–1.03	.152	1.03	1.00–1.06	.079	1.00	0.98–1.02	.953
Female sex (relative to male)	0.80	0.56–1.17	.251	0.74	0.41–1.33	.321	0.80	0.48–1.34	.397
Non-white (vs. white)	1.09	0.76–1.55	.648	1.27	0.69–2.32	.443	0.98	0.63–1.52	.926
Insurance (relative to private)									
Medicaid/Medicare	2.08	1.32–3.29	.002	1.94	0.92–4.06	.080	2.13	1.19–3.84	.012
None	2.41	1.45–3.99	.001	1.84	0.59–5.70	.290	2.59	1.42–4.72	.002
Other	2.00	1.20–3.33	.008	0.82	0.34–1.97	.663	3.32	1.74–6.34	.000
Smoking (> 10 pack-years)	1.09	0.72–1.65	.667	1.06	0.53–2.12	.869	1.06	0.62–1.80	.836
Alcohol use (any)	1.09	0.67–1.78	.723	1.68	0.77–3.65	.191	0.80	0.42–1.54	.504
TNM stage (relative to stage I)									
Stage II	1.41	0.87–2.30	.163	1.23	0.71–2.12	.452	NA		
Stage III	1.87	1.1–3.16	.020	NA			NA		
Stage IV	2.85	1.77–4.58	.000	NA			1.52	0.95–2.42	.082*
Adjuvant radiation	1.13	0.78–1.63	.519	1.13	0.59–2.18	.719	1.06	0.64–1.74	.821
Adjuvant chemotherapy	0.93	0.58–1.48	.755	NA			0.97	0.60–1.58	.912

**P* value for stage IV vs. stage III.
CI = confidence interval; NA = nonapplicable; TNM = tumor-node-metastasis.

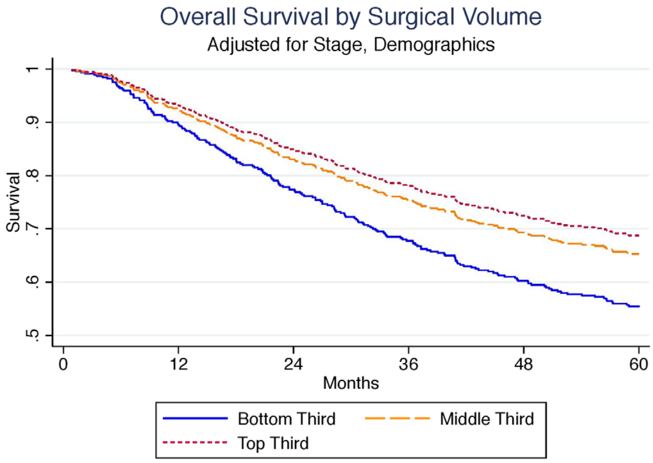

Fig. 3. Adjusted overall survival based on hospital volume type using a Cox proportional hazards model.

academic centers vs. 10% for both community cancer centers and community hospitals; $P < .001$).

We also compared the patient demographics, behaviors, tumor characteristics, and treatments across treatment centers with different volumes of HPV–head and neck cancer patients. Treatment centers in the bottom third by volume were significantly more likely to operate on white patients (81% white vs. 67% and 69% for middle and top-third centers, respectively; P = .009). Otherwise, there were no significant differences by age, sex, education, income, insurance, tobacco use, and alcohol use (Table I). Hospitals in the bottom third by volume operated on fewer patients with advanced T stage (33% vs. 61% for middle third and 58% for top-third; $P < .001$) and fewer patients with nodal metastases (21% vs. 48% for both middle and top third; $P < .001$). Hospitals in the middle third by volume operated on the most patients with an advanced T stage (40% vs. 23% of bottom third and 31% of top third; $P = .005$).

Survival Based on Both Treatment Center Type and Hospital Volume in Combined Model

We first examined whether treatment center type and hospital volume were associated with 5-year overall survival in a model that contained both variables of interest. We found that academic hospitals (HR = 0.82, 95% CI = 0.54–1.24) as well as community cancer centers (HR = 0.70, 95% CI = 0.47–1.03) had a nonsignificant trend toward better overall survival when compared to community hospitals that was independent of age, sex, race, tumor site, hospital affiliation, hospital volume, insurance status, tobacco use, alcohol use, overall stage, chemotherapy, and radiation therapy (Table II). Other predictors of poor survival included advanced stage and a lack of private insurance (Table II). We found that hospital affiliation and hospital volume were highly correlated (Pearson r = 0.48) in the combined model given that many of the high-volume hospitals were also academic centers or community cancer centers. We constructed separate models to examine the relative contributions of hospital affiliation and volume.

Survival Based on Hospital Affiliation

To examine the independent effect of hospital affiliation on overall survival, we created a model excluding hospital volume (Table III). Before adjustment, the 5-year overall survival was 0.56 (95% CI 0.48–0.63) for patients

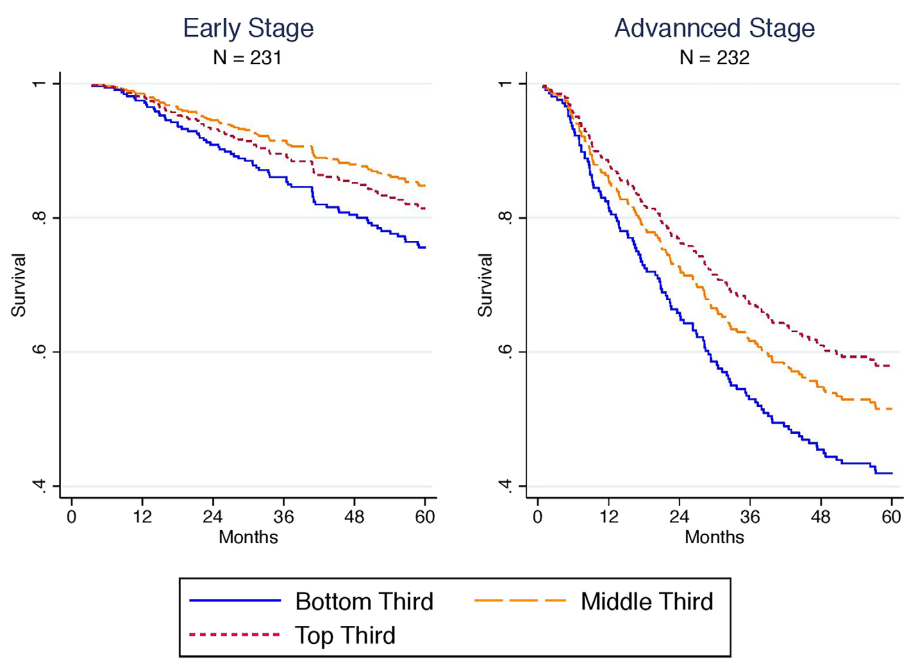

Fig. 4. Adjusted overall survival based on overall stage and hospital volume using a Cox proportional hazards model.

treated at academic centers, 0.64 (0.56–0.71) for patients treated at community cancer centers, and 0.61 (0.52–0.68) for patients treated at community hospitals. In the full models, we found that academic centers trended toward superior overall survival (HR 0.72, 95% CI = 0.50–1.04), and community cancer centers had significantly better overall survival (HR 0.68, 95% CI = 0.48–0.98) than community hospitals after adjusting for age, sex, race, tumor site, insurance status, tobacco use, alcohol use, overall stage, chemotherapy, and radiation therapy (Table III, Fig. 1).

This association differed by whether patients had early versus advanced stage cancer at diagnosis. For early stage patients, academic centers (P = .897) and community cancer centers (P = .867) did not have significantly different overall survival compared to community hospitals. For advanced stage patients, academic hospitals (HR 0.60, 95% CI = 0.37–0.95) and community cancer centers (HR 0.62, 95% CI = 0.39–1.00; P = .048) both had superior overall survival compared to community hospitals (Table III and Fig. 2).

Survival Based on Hospital Volume

We next examined whether the treatment center volume of HNSCC surgical cases was associated with overall survival. Before adjustment, the 5-year overall survival was 0.57 (95% CI 0.49–0.64) for patients treated in the bottom third of hospitals by surgical volume, 0.60 (0.52–0.67) for patients treated in the middle third, and 0.64 (0.56–0.72) for patients treated in the top third. In the full model top third (HR = 0.64, 95% CI = 0.42–0.96), treatment centers by volume were associated with significantly greater overall 5-year survival when compared to the bottom third sites after controlling for age, sex, race, tumor site, insurance status, tobacco use, alcohol use, overall stage, chemotherapy, and radiation therapy (Table IV, Fig. 3). Middle third treatment centers by volume had a nonsignificant trend toward better overall survival (HR = 0.71, 95% CI = 0.51–1.03) compared to bottom third hospitals in the adjusted model (Table IV). The effect of hospital volume on overall survival did not differ significantly by early versus advanced stage at diagnosis (Fig. 4).

DISCUSSION

Our study investigated whether the academic affiliation and surgical volume of treatment centers was associated with overall survival of HPV-negative HNSCC patients receiving surgery. The results demonstrated that academic and community cancer centers had greater overall 5-year survival compared to community hospitals (Fig. 1). Hospitals with a higher surgical volume also had a greater overall 5-year survival (Fig. 3). Importantly, we found that patients with advanced stage at diagnosis had a better 5-year overall survival when cared for in academic centers or community cancer centers, but there was not a significant difference among early stage patients (Fig. 2).

The results from our study are supported by several other studies that have shown better survival outcomes for patients with HNSCC treated at centers with higher case volume and academic affiliation, although these were limited to patients receiving primary radiotherapy for HNSCC.[18,24] Our study expands on the existing literature in head and neck oncology to include outcomes for patients treated surgically. Radiotherapy and surgery are both common treatment modalities for head and neck cancer, and outcomes for either may depend on a combination of provider expertise, facility resources, and access to multidisciplinary care. Surgical treatment also has different risks compared to radiotherapy, such as intraoperative or postoperative complications, which could potentially affect the relationship between academic affiliation, case volume, and survival outcomes.

There are several plausible explanations for the favorable mortality outcomes associated with academic affiliation. Academic centers tend to be large tertiary care centers with multidisciplinary treatment groups and the latest advancements in treatment. Multidisciplinary care is especially important for patients with advanced malignancies, who often receive multiple treatment modalities.[25–27] Academic centers may also attract subspecialty experts with clinical and research careers devoted to head and neck oncologic surgery, which could lead to more nuanced treatment plans. Additionally, academic centers may have better access to other fellowship-trained head and neck surgeons for consultation and assistance in the operating room when needed. These mechanisms are largely speculative, and more research is needed to uncover differences in the surgical treatment between academic- and community-based centers.

Interestingly, community cancer centers had similar survival outcomes compared to academic centers for our sample, and both groups displayed superiority over community hospitals. There may be several reasons for this finding. First, many community cancer centers have adopted a multidisciplinary model of treatment, and these centers have invested in infrastructure to support advanced cancer therapy.[25–27] Second, academic centers are relatively concentrated to the central and eastern aspects of our state. In the western half of the state, a large community cancer center has grown to fill this void and has established itself as a high-volume center for HNSCC with multiple fellowship-trained head and neck surgeons. Notably, this single community cancer center had the highest total case volume during the study period.

Our finding that higher surgical volume is associated with better survival outcomes in HNSCC is consistent with other studies in literature across a variety of conditions.[10–12,28–30] Higher case volume likely leads to more experience for the surgeons and greater exposure to both routine and difficult cases. It is plausible that surgeons with more experience could obtain better surgical margins and have a lower incidence of complications. Indeed, previous studies have demonstrated that experienced surgeons tend to have superior results in multiple types of operations.[15,31–34] In addition, higher volume centers may have more advanced surgical options and treatment modalities, which may result in better overall survival particular for advanced stage disease.

There are several unique strengths to our study. To our knowledge, this is the first statewide study that examines surgical outcomes for HPV-negative HNSCC by treatment center and hospital volume. We used a large population-based cohort to examine overall survival while adjusting for patient demographics, clinical characteristics, and socioeconomic factors. Although most published databases use patients primarily treated at academic centers, CHANCE captured patients from a state cancer registry and was able to include patients who had been treated at 39 different sites. Finally, full 5-year follow-up was available for all patients.

There are several limitations as well. We only investigated patients who received surgical treatment with or without adjuvant therapy; we did not include patients who received chemotherapy or radiation alone. In addition, the academic affiliations of treatment centers for adjuvant therapy were not recorded. Although we adjusted for presurgical variables, such as patient demographics, insurance status, and tumor characteristics, there may be other unmeasured confounders that affected survival, such as the type of surgery and tumor margin status. Nonetheless, differences in these variables are likely distributed relatively evenly across treatment centers. A further limitation is the use of the 2006 federal poverty level to approximate income cutoffs. It is now recognized that the FPL underestimates a family's ability to meet basic needs because, although it adjusts for inflation, it does not take into account the rising costs of healthcare, housing, or childcare.[23] Better cutoff values would ideally use measurements such as the Living Income Standard,[23] but these were unavailable at the time of data collection in 2006. In addition, although we conclude that patients have worse outcomes at hospitals with a lower surgical volume, we are unable to generate an objective definition of how many surgical cases constitutes a low-volume center. The CHANCE cohort provides a good approximation of the relative volume of surgical HNSCC cases over the study period, but the study authors do not have access to the true case volume per year of each institution. A final limitation is that the associations between survival and the academic affiliation and hospital volume variables did not reach significance when both were used in the same model, although each had a trend toward significance. This statistical effect is likely caused by both correlated variables adjusting for each other; associations with each variable and survival were significant when the other was removed. Despite these limitations, our study adds an important contribution to the medical literature on optimizing HNSCC surgical outcomes and underscores the importance of centralization of cancer care.

CONCLUSION

This is the first statewide study to investigate the survival of surgically treated HPV- HNSCC patients in relation to treatment center type and surgical volume. Our study suggests that patients treated at academic centers and hospitals with higher surgical volume have favorable survival. Future research is needed to better understand the mechanisms underlying this association.

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