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Is there a difference in staging and treatment of head and neck squamous cell tumors between tertiary care and community-based institutions?

Short title: Institutional cancer staging differences

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This study was presented at the Combined American Head and Neck Society Section Meetings, Boston, Massachusetts, April 24, 2015.

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ABSTRACT

Objective: To characterize the differences in the staging and treatment of patients with head and neck squamous cell carcinoma between a tertiary care center and community-based practices.

Methods: This study is a retrospective chart review of 943 adult patients with head and neck squamous cell cancer presenting to a tertiary care center between 2008 and 2014 as part of the University of Michigan Head and Neck Cancer Specialized Program of Research Excellence (UM HN-SPORE) database. Demographic information, diagnostic testing, staging information, and treatment recommendations were recorded.

Results: Of 943 patients reviewed, 159 had documentation of tumor stage that was assigned by the community-based practice. Of these, 53% had a tumor staging change made at the tertiary care center, with 43% of patients upstaged and 10% of patients downstaged. 51% received different treatment than had previously been offered at the community-based practice, although only 31% of these patients had a change in tumor staging.

Conclusion: Over half of patients with head and neck squamous cell carcinoma who are evaluated at a tertiary care center after the initial evaluation at a community-based practice have their tumors staged differently, with the majority upstaged. A significant number of these patients also received different treatment than was initially offered at the referring practice. Future studies are required to determine whether these differences have an effect on tumor recurrence and patient survival rates.

Key Words: adult head and neck squamous cell carcinoma, neoplasm staging, tertiary care center

Level of Evidence: 2c (Outcomes Research)

Introduction

In the assessment of head and neck cancer, accurate staging is imperative because prognosis and treatment are directly related to the tumor stage assigned to each patient.¹ Tumor staging allows meaningful discussion between members of the patient care team to achieve an appropriate and customized treatment plan for each patient.^{2,3} Originating from the American Joint Committee on Cancer (AJCC) in conjunction with the International Union Against Cancer (UICC), TNM classification of head and neck cancer⁴ is now the standard staging system used in clinical practice and the published literature.¹

Despite the importance of initial staging, relatively few studies have examined differences in the staging process or compared tumor stage assignments between institutions. Although studies have shown a disparity in survival rates of head and neck cancer patients between different institutions, no study has compared tumor staging assignments to identify staging differences and restaging between institutions.^{5,6}

We hypothesized that there are institutional differences in tumor stage assignment. We sought to quantify these differences and to identify patient-specific factors associated with these differences and secondarily to compare differences in treatment recommendations. We designed a study to compare institutional tumor staging by examining patients diagnosed with head and neck squamous cell carcinoma at community-based practices who subsequently presented to our tertiary care academic center. We sought to identify whether staging differences identified are a result of patient-specific factors, if different treatment was offered at the tertiary care center, and if treatment differences were related to staging changes.

Materials and Methods

A retrospective chart review was conducted on patients within the University of Michigan Head and Neck Cancer Specialized Program of Research Excellence (UM HN-SPORE). The UM HN-

SPORE database consists of patients who have presented to the University of Michigan for evaluation and treatment of head and neck cancers, and consented to be in research studies regarding factors impacting treatment and survival of their cancers. We identified patients who had previously been staged at a community-based practice and had subsequently been staged at our tertiary care center, the University of Michigan. We included all patients with HNSCC. Upon registration into the UM HN-SPORE database, demographic information on each patient had been collected along with diagnosis, treatment, and outcome measures. Race was self-reported by patients. For the purposes of this study, the data collection also included chart review of referral documentation to determine tumor staging by community-based practice, treatment offered by the community practice, and whether the patient then presented to the tertiary care center for assumption of care versus a second opinion. Descriptive statistics were calculated on demographics, changes in staging, reasons for changes in stage, and treatment offered. Demographic differences were analyzed between patients with staging changes, compared to those with no staging change, using Fisher's Exact test at a significance level of $\alpha = 0.05$. Statistical analyses were performed using STATA SE 12 (StataCorp, College Station, Texas) statistical software.

Results

In total, 943 patients were reviewed. Of these, 159 patients had complete documentation from the community-based practice including tumor staging; this patient subset was the main group analyzed. The mean age of these patients was 60 years. 77% of patients were male, 23% female, and the vast majority were European American/White (91%) with the remainder including 6% African American/Black, 1% Asian, 2% American Indian/Eskimo/ Aleutian, and 1% other. Wait-time between staging of patient at the community-based practice and initial presentation to

the tertiary care center was on average 14.7 days. Complete patient characteristics and tumor sites and stages as determined by the tertiary care center are demonstrated in **Table 1 and 2**.

Following evaluation at the tertiary care center, 85 (53%) patients were re-assigned a different tumor stage, with 69 (43%) patients upstaged and 16 (10%) patients downstaged [**Table 3**]. Of the patients with staging changes, 45 (53%) had been evaluated by a multidisciplinary tumor board at the tertiary care institute. Of this subset, 24 patients underwent stage change based on the tumor board recommendations, with the other 21 patients having had an initial staging that was already changed from that given at the referring institute during tertiary care clinic evaluation. Patients with HNSCC of the oropharynx and of the tongue were most commonly upstaged compared to other tumor sites [**Figure 1**]. Reasons for staging changes included differences in clinical exam at the tertiary care center (e.g. lymph node determined to be larger), differences in radiology reviews (e.g. an additional enlarged lymph node identified), and new imaging taken. Patient characteristics including demographics, disease recurrence, and persistence were compared between those that had tumor staging changes made at the tertiary care center and those that did not. Fisher Exact testing, between patients with tumor staging change and those without, did not reveal any statistically significant differences [**Table 4**].

Treatment offered at the community-based practice was then compared to treatment received by the patient at the tertiary care center. Of the 159 patients with outside records analyzed, 78 patients had documentation of specific treatment recommendations at the community-based practice and treatment received at the tertiary care center. Of these, 37 (47%) patients received treatment that was different than what was recommended by the community-based practice. Interestingly, only 18 of these patients, or roughly half, had staging changes made. Thus, 19 patients received treatment that was different than initially recommended by the community-based practice even without having undergone a change in tumor staging status. Also of

note, of the 37 patients with a treatment change, 20 (54%) had been referred for a second opinion, not specifically for assumption of clinical care.

Discussion

Tumors of the head and neck are expected to be clinically staged under AJCC guidelines,¹ but our data reveals that HNSCC tumors are often staged differently at tertiary care centers compared to community-based practices. In patients analyzed in this study, over half of tumors were restaged. The majority were restaged with a more advanced stage by the tertiary care center, despite relatively minimal time between the referral and tertiary care center evaluation. Additionally, many of the patients had a change in treatment received at the tertiary care center compared to what was recommended by the community-based practice. Roughly half of these patients had their tumor staging changed prior to treatment. The other half did not, meaning the change in treatment recommended was due to a factor outside of tumor staging. Details of why each patient's treatment regimen was recommended at the community-based hospital were unable to be characterized, though presumably related to evaluation of clinical characteristics and imaging/diagnostic studies.

The differences in tumor staging between community-based practices and tertiary care centers may be attributed to overall volume and experience with head and neck cancer, as well as the availability of additional specialists including highly trained radiologists and cytopathologists available through multidisciplinary tumor boards to clarify clinically challenging cases. Previous literature has examined overall differences in survival of head and neck cancer patients at different treating institutions.^{5,6} One such study evaluating patients with local advanced head and neck cancer undergoing definitive radiotherapy found that treatment at high-volume facilities and academic centers is independently associated with improved survival, using the National Cancer Data Base to include over 46,000 patients.⁷ When determining what led to the difference, studies

have implicated factors such as the volume of treatments rendered at the facilities⁸, technical expertise⁹ as well as multidisciplinary team management^{3,9}. In one study examining 1195 Medicare patients with advanced head and neck cancer treated at high and low volume centers, patients were found to have nearly statistically significant better survival at high volume hospitals despite no association found in receiving multimodality therapy.¹⁰ This implies that survival-promoting features of high volume hospitals extends beyond guideline adherence. These studies overall also imply a difference in overall patient care across institutions and may explain the observed negative effect on survival noted on the literature.^{3,6} Therefore, it is apparent that further exploration of the staging process represents a major avenue for identifying factors that affect the institutional-based outcome differences.

A typical diagnostic work-up to determine staging traditionally involves a thorough history and physical examination, followed by additional testing which may include endoscopy of the upper aerodigestive tract, imaging via computed tomography (CT), magnetic resonance imaging (MRI), ultrasonography (US), fine needle aspiration cytology (FNAC) of a neck mass and incisional biopsy of the primary tumor¹¹⁻¹³. While these additional tests can lead to greater accuracy in determining disease extent, clinical judgment of the practitioner or general institutional guidelines may conclude that additional testing is unnecessary to accurately stage the tumor. Therefore, a wide range of test utilization between practitioners and institutions is likely. Recently, Lewis et al have analyzed pre-referral staging at community institutions for adherence to the National Comprehensive Cancer Network (NCCN) guidelines. Their data showed significant deviation from the guidelines by community-based practices, leading to inadequate surgical treatment and misdiagnosis for patients treated only at community institutions¹⁴.

At our tertiary care center, staging is based on NCCN guidelines and is often confirmed or augmented via evaluation by a multidisciplinary tumor board. In this dataset, of 159 patients identified, 84 (53%) underwent tumor board evaluation. Community-based practices often do not

have such easy and coordinated access to specialists of other disciplines which can significantly aid in the evaluation of tumors, especially in more complicated cases or areas of tumor that are more rare, therefore very infrequently seen in the community. The positive effect of multidisciplinary tumor boards in impacting patient assessment and management has been studied in many oncological settings, from head and neck cancer to breast, urologic, gastrointestinal, and gynecological cancers.¹⁵⁻²⁰ A recent systematic review reporting that between 4% to 45% of patients discussed at multidisciplinary team meetings had changes in diagnostic reports.²¹ Additionally, the clinical impact of multidisciplinary head and neck tumor board has been previously studied, examining discussion of 120 consecutive patients which revealed that 27% of patients had some change in tumor diagnosis, stage, or treatment plan.¹⁵ Our study has gone a step further in directly assessing the referral documentation and work up at community-based practices, as well as patient demographic factors. Our findings support the prior study's conclusion that multidisciplinary approaches to patient care affect staging and treatment recommendations.

Regarding staging, our data reveals that particular tumor sites may lead to increased staging discrepancies, as 68% of oropharynx tumors were re-staged at the tertiary care center compared to 49% of oral cavity tumors and 41% of larynx tumors. This may relate to the changes in oropharynx tumor staging with the important recognition of differences in survival for Human Papilloma Virus (HPV)-associated tumors.²² As new staging systems have arisen, academic centers may have earlier access to this information and process than community-based centers. Additionally, oropharyngeal tumors can be difficult to assess radiologically in regards to involvement in extrinsic musculature of the tongue or pterygoids which highly trained radiologists can aid with at academic centers particularly through multidisciplinary tumor boards. Community-based centers may not have the same access. With classification of HPV tumors, cytopathology also plays a crucial role. Academic centers may have better access to more specialized cytopathologists as well. The interpretation of diagnostic studies is subject to high variability between institutions

and between providers, possibly leading to the deviations. Previous studies have indicated that reinterpretation of imaging in the setting of a multidisciplinary cancer center has a significant effect on staging, management, and prognosis^{9,23,24}. As our data shows, roughly half of the patients evaluated with staging changes had this change made in the context of review by a multidisciplinary tumor board.

There are several limitations of this study. First, the database was limited to patients who sought evaluation at a tertiary care center. This group may inherently be more difficult to examine and diagnose, leading to greater discrepancy in staging. Additionally, referral documents used in chart review may not have included all outside clinical notes which community-based practices may have used to determine tumor stage. The patient group was fairly diverse with respect to tumor site and stage, making it difficult to identify any differences in outcome or whether differences in patient characteristics could be confounding. It is also possible that patients may not have been clinically understaged, but rather that the disease progressed by the time they were referred to our institution. However, given our finding that patients were subsequently evaluated at the tertiary care center on average only 14 days after their referral encounter, this is less likely to present a significant limitation. Additionally, it could be argued that because this study is limited to patients presenting to a tertiary care center, that community-based practices may not have conducted additional tests or diagnostic studies out of an assumption that the tertiary care center would assume care and give a final stage and recommendation. However, as noted above, among the group of patients with changes in treatment recommendations, 54% had presented for a second opinion, without which they presumably would have underwent the initial treatment offered by the referring institution. Finally, there is an underlying assumption that the tertiary care center was fully adherent to NCCN guidelines in staging; this study did not officially validate the tertiary care center staging concordance with NCCN guidelines, and discrepancies therefore could exist.

Future studies should examine the differences in exactly how community-based practices versus tertiary institutions stage patients, specifically focusing on the tests ordered at each institution to aid with staging. Ultimately, survival based on the changes in staging and treatment modalities offered to patients at different institutions should be examined in order to determine overall and disease free survival.

Conclusion

Over half of patients with HNSCC who present to tertiary care centers from community-based practices have their tumors' stage changed, with the majority upstaged. Interestingly, in nearly half of patients receiving treatment that is different than was initially recommended at the community-based practice; only half of these patients had undergone a tumor staging change. Future studies are required to determine whether these differences result in an effect on patient outcomes, including recurrence and survival rates.

References

1. Patel SG, Shah JP. TNM staging of cancers of the head and neck: striving for uniformity among diversity. *CA: a cancer journal for clinicians* 2005; 55:242-258.
2. Patel NN, Faris C, Upile T. Getting the basics right-staging in head and neck cancer. *Head & neck oncology* 2009; 1:16.
3. Friedland PL, Bozic B, Dewar J, Kuan R, Meyer C, Phillips M. Impact of multidisciplinary team management in head and neck cancer patients. *British journal of cancer* 2011; 104:1246-1248.
4. Edge SB, Compton CC. The American Joint Committee on Cancer: the 7th edition of the AJCC cancer staging manual and the future of TNM. *Annals of surgical oncology* 2010; 17:1471-1474.
5. Lassig AA, Joseph AM, Lindgren B, et al. The effect of treating institution on outcomes in head and neck cancer. *Otolaryngology--head and neck surgery : official journal of American Academy of Otolaryngology-Head and Neck Surgery* 2012; 147:1083-1092.
6. Sdvizhkov AM, Kozhanov AG, Shatskaia N, Iadykov OA. [Delayed results of the treatment of patients with laryngeal cancer in Moscow]. *Vestnik otorinolaringologii* 2009:20-22.
7. David JM, Ho AS, Luu M, Yoshida EJ, Kim S, Mita AC, Scher KS, Shiao SL, Tighiouart M, Zumsteg ZS. Treatment at high-volume facilities and academic centers is independently associated with improved survival in patients with locally advanced head and neck cancer. *Cancer* 2017; 123:3933-3942.
8. Chen AY, Fedewa S, Pavluck A, Ward EM. Improved survival is associated with treatment at high-volume teaching facilities for patients with advanced stage laryngeal cancer. *Cancer* 2010; 116:4744-4752.
9. Karakohyun-Celik O, AM, Olmezoglu A, Buyukpolat MY, Ozkok S et al. Practice patterns for oropharyngeal cancer in radiation oncology centers of Turkey. *Tumori* 2014:284-288.

0. Sharma A, Schwartz SM, Mendez E. Hospital volume is associated with survival but not multimodality therapy in Medicare patients with advanced head and neck cancer. *Cancer* 2013; 119:1845-1852.
1. Braunius WW, van Gils CH, Rosenberg AJ, Hordijk GJ, Moons KG. Observing stage-shifts in head and neck squamous cell carcinoma from initial clinical outpatient staging to definite clinical tumour board staging using radiological and endoscopical investigations: will less do? *Clinical otolaryngology : official journal of ENT-UK ; official journal of Netherlands Society for Oto-Rhino-Laryngology & Cervico-Facial Surgery* 2011; 36:352-360.
2. Broumand V, Lozano TE, Gomez JA. Evaluation and staging of oral cancer. *Oral and maxillofacial surgery clinics of North America* 2006; 18:435-444.
3. Lubek JE, Clayman L. An update on squamous carcinoma of the oral cavity, oropharynx, and maxillary sinus. *Oral and maxillofacial surgery clinics of North America* 2012; 24:307-316, x.
4. Lewis CM, Hessel AC, Roberts DB et al. Prereferral head and neck cancer treatment: compliance with national comprehensive cancer network treatment guidelines. *Archives of otolaryngology--head & neck surgery* 2010; 136:1205-1211.
5. Wheless SA, McKinney KA, Zanation AM. A prospective study of the clinical impact of a multidisciplinary head and neck tumor board. *Otolaryngol Head Neck Surg* 2010; 143:650-654.
6. Kesson EM, Allardice GM, George WD, et al. Effects of multidisciplinary team working on breast cancer survival: retrospective, comparative, interventional cohort study of 13 722 women. *BMJ* 2012; 344:e2718.
7. Kurpad R, Kim W, Rathmell WK, et al. A multidisciplinary approach to the management of urologic malignancies: does it influence diagnostic and treatment decisions? *Urol Oncol* 2011; 29:378-82.

8. van Hagen P, Spaander MC, van der Gaast A, et al. Impact of a multidisciplinary tumour board meeting for upper-GI malignancies on clinical decision making: a prospective cohort study. *Int J Clin Oncol* 2013; 18:214–9.
9. Oxenberg J, Papenfuss W, Esemuede I, et al. Multidisciplinary cancer conferences for gastrointestinal malignancies result in measureable treatment changes: a prospective study of 149 consecutive patients. *Ann Surg Oncol* 2015; 22:1533–9.
0. Greer HO, Frederick PJ, Falls NM, et al. Impact of a weekly multidisciplinary tumor board conference on the management of women with gynecologic malignancies. *Int J Gynecol Cancer* 2010; 20:1321–5.
1. Pillay B, Wootten AC, Crowe H, et al. The impact of multidisciplinary team meetings on patient assessment, management and outcomes in oncology settings: a systematic review of the literature. *Cancer Treat Rev* 2016; 42:56–72.
2. Huang SH, O'Sullivan B. Overview of the 8th Edition TNM Classification for Head and Neck Cancer. *Curr Treat Options Oncol* 2017; 18:40.
3. Loevner LA, Sonners AI, Schulman BJ et al. Reinterpretation of cross-sectional images in patients with head and neck cancer in the setting of a multidisciplinary cancer center. *AJNR American journal of neuroradiology* 2002; 23:1622-1626.
4. Lysack JT, Hoy M, Hudon ME et al. Impact of neuroradiologist second opinion on staging and management of head and neck cancer. *Journal of otolaryngology - head & neck surgery = Le Journal d'oto-rhino-laryngologie et de chirurgie cervico-faciale* 2013; 42:39.

Table 1. Patient Demographics

Patient Characteristics	Percent of total (N = 159)
Sex	
Male	77
Female	23
Age (Years)	60
Race	
European American/White	91
African American/Black	6
Asian	1
American Indian/Eskimo/Aleutian	2
Other	1
Baseline tobacco status	
Never smoker	25
Current in past 12 mo	47
Former smoker >12mo	28
Baseline alcohol status	
Never drinker	8
Current drinker	69
Former drinker >12mo	23
BMI Category	
Underweight	7

Normal	40	327
Overweight	32	328
Obese	21	329
Recurrence		
Alive, no recurrence	77	
Recurred or persistence	23	
Disease Persistence		
No disease present after treatment	88	
Disease present after treatment completed or palliative at baseline	12	
Education Level		
	(N = 121)	
Less than High School	6	
High School or GED	30	
Some College	37	
4 year degree or greater	27	
Marital Status		
	(N = 155)	
Married	67	
Widowed	10	
Separated or divorced	8	
Never married	14	
Median Household Income (\$)		
	48,202.00	
Average Wait Time		
	14.7 days	
	(Range 0-163 days)	

Table 2. Patient tumor sites and stages determined by tertiary care center

Tumor Site	Stage 1	Stage 2	Stage 3	Stage 4	Total
Larynx	10	4	4	14	32
Oral cavity	7	11	8	27	53
Oropharynx	2	0	8	49	59
Hypopharynx	0	0	1	3	4
Nasopharynx	0	0	0	1	1
Skull base	0	0	0	1	1
Unknown primary	0	0	1	8	9
TOTAL	19	15	22	103	159

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Table 3. Tumor staging changes made, by tumor site

Tumor Site	No Difference	Stage Difference		Percent Staged Differently
		Upstaged	Downstaged	
Larynx	19	9	4	41
Oral cavity	27	18	8	49
Oropharynx	19	37	3	68
Hypopharynx	3	1	0	25
Nasopharynx	0	1	0	100
Skull base	1	0	0	0
Unknown primary	5	3	1	44
TOTAL	74	69	16	53

Table 4. Patient characteristics of patients with and without tumor stage change

Patient Characteristics	No Stage Difference	Stage Difference			P-value*
		Upstaged	Downstaged	Total	
Sex					0.109
Male	53	58	11	69	
Female	21	11	5	16	
Race					0.42
European American/White	65	65	15	80	
African American/Black	6	3	0	3	
Asian	1	0	0	0	
American Indian/Eskimo/Aleutian	1	1	1	2	
Other	1	0	0	0	
Baseline tobacco status					0.20
Never smoker	14	22	4	26	
Current in past 12 mo	39	27	8	35	
Former smoker >12mo	21	20	4	24	
Baseline alcohol status					0.97
Never drinker	5	6	1	7	
Current drinker	52	45	13	58	
Former drinker >12mo	17	18	2	20	
BMI Category					0.61
Underweight	7	4	0	4	
Normal	27	26	10	36	

Overweight	25	23	3	26	
Obese	15	16	3	19	
Recurrence					0.54
Alive, no recurrence	57	53	12	65	
Recurred or persistence	17	16	4	20	
Disease Persistence					0.57
No disease present after treatment	65	62	13	75	
Disease present after treatment completed or palliative at baseline	9	7	3	10	
Education Level					0.93
Less than High School	3	2	2	4	
High School or GED	19	11	6	17	
Some College	21	21	3	24	
4 year degree or greater	17	13	3	16	
Marital Status					0.39
Married	51	46	7	53	
Widowed	5	7	4	11	
Separated or divorced	8	4	1	5	
Never married	9	10	3	13	

*Fisher exact test was conducted for each category comparing the number of patients with no stage difference to the total number of patients with a stage difference, either upstaged or downstaged

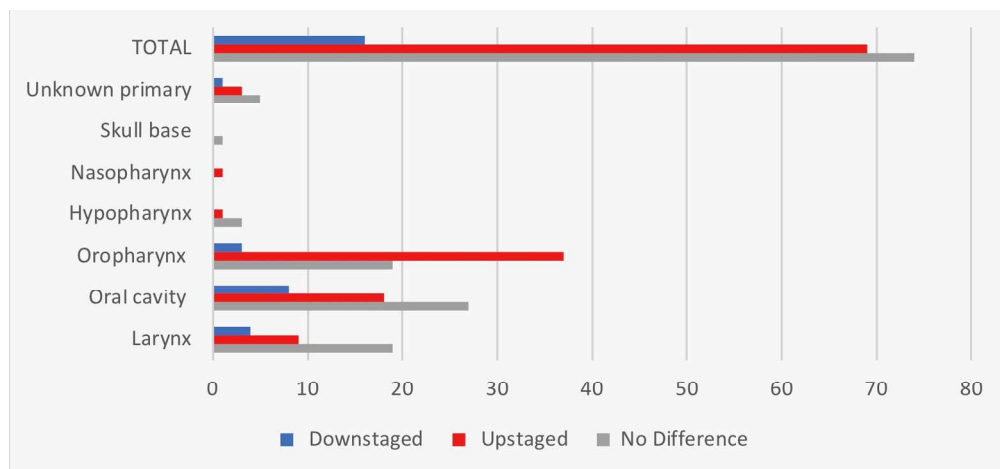


Figure 1. Tumor staging changes made, by tumor site

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Results: Of 943 patients reviewed, 159 had documentation of tumor stage that was assigned by the community-based practice. Of these, 53% had a tumor staging change made at the tertiary care center, with 43% of patients upstaged and 10% of patients downstaged. 51% received different treatment than had previously been offered at the community-based practice, although only 31% of these patients had a change in tumor staging.

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Level of Evidence: 2c (Outcomes Research)

Introduction

In the assessment of head and neck cancer, accurate staging is imperative because prognosis and treatment are directly related to the tumor stage assigned to each patient.¹ Tumor staging allows meaningful discussion between members of the patient care team to achieve an appropriate and customized treatment plan for each patient.^{2,3} Originating from the American Joint Committee on Cancer (AJCC) in conjunction with the International Union Against Cancer (UICC), TNM classification of head and neck cancer⁴ is now the standard staging system used in clinical practice and the published literature.¹

Despite the importance of initial staging, relatively few studies have examined differences in the staging process or compared tumor stage assignments between institutions. Although studies have shown a disparity in survival rates of head and neck cancer patients between different institutions, no study has compared tumor staging assignments to identify staging differences and restaging between institutions.^{5,6}

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In total, 943 patients were reviewed. Of these, 159 patients had complete documentation from the community-based practice including tumor staging; this patient subset was the main group analyzed. The mean age of these patients was 60 years. 77% of patients were male, 23% female, and the vast majority were European American/White (91%) with the remainder including 6% African American/Black, 1% Asian, 2% American Indian/Eskimo/ Aleutian, and 1% other. Wait-time between staging of patient at the community-based practice and initial presentation to

the tertiary care center was on average 14.7 days. Complete patient characteristics are demonstrated in Table 1.

Following evaluation at the tertiary care center, 85 (53%) patients were re-assigned a different tumor stage, with 69 (43%) patients upstaged and 16 (10%) patients downstaged [Table 2]. Of the patients with staging changes, 45 (53%) had been evaluated by a multidisciplinary tumor board at the tertiary care institute. Of this subset, 24 patients underwent stage change based on the tumor board recommendations, with the other 21 patients having had an initial staging that was already changed from that given at the referring institute during tertiary care clinic evaluation. Patients with HNSCC of the oropharynx and of the tongue were most commonly upstaged compared to other tumor sites. Reasons for staging changes included differences in clinical exam at the tertiary care center (e.g. lymph node determined to be larger), differences in radiology reviews (e.g. an additional enlarged lymph node identified), and new imaging taken. Patient characteristics including demographics, disease recurrence, and persistence were compared between those that had tumor staging changes made at the tertiary care center and those that did not, revealing that tumors of the oropharynx had the highest percentage (68%) of restaging. [Table 3]. Fisher Exact testing, between patients with tumor staging change and those without, did not reveal any statistically significant differences.

Treatment offered at the community-based practice was then compared to treatment received by the patient at the tertiary care center. Of the 159 patients with outside records analyzed, 78 patients had documentation of specific treatment recommendations at the community-based practice and treatment received at the tertiary care center. Of these, 37 (47%) patients received treatment that was different than what was recommended by the community-based practice. Interestingly, only 18 of these patients, or roughly half, had staging changes made. Thus, 19 patients received treatment that was different than initially recommended by the community-based practice even without having undergone a change in tumor staging status. Also of

note, of the 37 patients with a treatment change, 20 (54%) had been referred for a second opinion, not specifically for assumption of clinical care.

Discussion

Tumors of the head and neck are expected to be clinically staged under AJCC guidelines,¹ but our data reveals that HNSCC tumors are often staged differently at tertiary care centers compared to community-based practices. In patients analyzed in this study, over half of tumors were restaged. The majority were restaged with a more advanced stage by the tertiary care center, despite relatively minimal time between the referral and tertiary care center evaluation. Additionally, many of the patients had a change in treatment received at the tertiary care center compared to what was recommended by the community-based practice. Roughly half of these patients had their tumor staging changed prior to treatment. The other half did not, meaning the change in treatment recommended was due to a factor outside of tumor staging. Details of why each patient's treatment regimen was recommended at the community-based hospital were unable to be characterized, though presumably related to evaluation of clinical characteristics and imaging/diagnostic studies.

The differences in tumor staging between community-based practices and tertiary care centers may be attributed to overall volume and experience with head and neck cancer, as well as the availability of additional specialists including highly trained radiologists and cytopathologists available through multidisciplinary tumor boards to clarify clinically challenging cases. Previous literature has examined overall differences in survival of head and neck cancer patients at different treating institutions.^{5,6} One such study evaluating patients with local advanced head and neck cancer undergoing definitive radiotherapy found that treatment at high-volume facilities and academic centers is independently associated with improved survival, using the National Cancer Data Base to include over 46,000 patients.⁷ When determining what led to the difference, studies

have implicated factors such as the volume of treatments rendered at the facilities⁸, technical expertise⁹ as well as multidisciplinary team management^{3,9}. In one study examining 1195 Medicare patients with advanced head and neck cancer treated at high and low volume centers, patients were found to have nearly statistically significant better survival at high volume hospitals despite no association found in receiving multimodality therapy.¹⁰ This implies that survival-promoting features of high volume hospitals extends beyond guideline adherence. These studies overall also imply a difference in overall patient care across institutions and may explain the observed negative effect on survival noted on the literature.^{3,6} Therefore, it is apparent that further exploration of the staging process represents a major avenue for identifying factors that affect the institutional-based outcome differences.

A typical diagnostic work-up to determine staging traditionally involves a thorough history and physical examination, followed by additional testing which may include endoscopy of the upper aerodigestive tract, imaging via computed tomography (CT), magnetic resonance imaging (MRI), ultrasonography (US), fine needle aspiration cytology (FNAC) of a neck mass and incisional biopsy of the primary tumor¹¹⁻¹³. While these additional tests can lead to greater accuracy in determining disease extent, clinical judgment of the practitioner or general institutional guidelines may conclude that additional testing is unnecessary to accurately stage the tumor. Therefore, a wide range of test utilization between practitioners and institutions is likely. Recently, Lewis et al have analyzed pre-referral staging at community institutions for adherence to the National Comprehensive Cancer Network (NCCN) guidelines. Their data showed significant deviation from the guidelines by community-based practices, leading to inadequate surgical treatment and misdiagnosis for patients treated only at community institutions¹⁴.

At our tertiary care center, staging is based on NCCN guidelines and is often confirmed or augmented via evaluation by a multidisciplinary tumor board. In this dataset, of 159 patients identified, 84 (53%) underwent tumor board evaluation. Community-based practices often do not

have such easy and coordinated access to specialists of other disciplines which can significantly aid in the evaluation of tumors, especially in more complicated cases or areas of tumor that are more rare, therefore very infrequently seen in the community. The positive effect of multidisciplinary tumor boards in impacting patient assessment and management has been studied in many oncological settings, from head and neck cancer to breast, urologic, gastrointestinal, and gynecological cancers.¹⁵⁻²⁰ A recent systematic review reporting that between 4% to 45% of patients discussed at multidisciplinary team meetings had changes in diagnostic reports.²¹ Additionally, the clinical impact of multidisciplinary head and neck tumor board has been previously studied, examining discussion of 120 consecutive patients which revealed that 27% of patients had some change in tumor diagnosis, stage, or treatment plan.¹⁵ Our study has gone a step further in directly assessing the referral documentation and work up at community-based practices, as well as patient demographic factors. Our findings support the prior study's conclusion that multidisciplinary approaches to patient care affect staging and treatment recommendations.

Regarding staging, our data reveals that particular tumor sites may lead to increased staging discrepancies, as 68% of oropharynx tumors were re-staged at the tertiary care center compared to 49% of oral cavity tumors and 41% of larynx tumors. This may relate to the changes in oropharynx tumor staging with the important recognition of differences in survival for Human Papilloma Virus (HPV)-associated tumors.²² As new staging systems have arisen, academic centers may have earlier access to this information and process than community-based centers. Additionally, oropharyngeal tumors can be difficult to assess radiologically in regards to involvement in extrinsic musculature of the tongue or pterygoids which highly trained radiologists can aid with at academic centers particularly through multidisciplinary tumor boards. Community-based centers may not have the same access. With classification of HPV tumors, cytopathology also plays a crucial role. Academic centers may have better access to more specialized cytopathologists as well. The interpretation of diagnostic studies is subject to high variability between institutions

and between providers, possibly leading to the deviations. Previous studies have indicated that reinterpretation of imaging in the setting of a multidisciplinary cancer center has a significant effect on staging, management, and prognosis^{9,23,24}. As our data shows, roughly half of the patients evaluated with staging changes had this change made in the context of review by a multidisciplinary tumor board.

There are several limitations of this study. First, the database was limited to patients who sought evaluation at a tertiary care center. This group may inherently be more difficult to examine and diagnose, leading to greater discrepancy in staging. Additionally, referral documents used in chart review may not have included all outside clinical notes which community-based practices may have used to determine tumor stage. The patient group was fairly diverse with respect to tumor site and stage, making it difficult to identify any differences in outcome or whether differences in patient characteristics could be confounding. It is also possible that patients may not have been clinically understaged, but rather that the disease progressed by the time they were referred to our institution. However, given our finding that patients were subsequently evaluated at the tertiary care center on average only 14 days after their referral encounter, this is less likely to present a significant limitation. Additionally, it could be argued that because this study is limited to patients presenting to a tertiary care center, that community-based practices may not have conducted additional tests or diagnostic studies out of an assumption that the tertiary care center would assume care and give a final stage and recommendation. However, as noted above, among the group of patients with changes in treatment recommendations, 54% had presented for a second opinion, without which they presumably would have underwent the initial treatment offered by the referring institution. Finally, there is an underlying assumption that the tertiary care center was fully adherent to NCCN guidelines in staging; this study did not officially validate the tertiary care center staging concordance with NCCN guidelines, and discrepancies therefore could exist.

Future studies should examine the differences in exactly how community-based practices versus tertiary institutions stage patients, specifically focusing on the tests ordered at each institution to aid with staging. Ultimately, survival based on the changes in staging and treatment modalities offered to patients at different institutions should be examined in order to determine overall and disease free survival.

Conclusion

Over half of patients with HNSCC who present to tertiary care centers from community-based practices have their tumors' stage changed, with the majority upstaged. Interestingly, in nearly half of patients receiving treatment that is different than was initially recommended at the community-based practice; only half of these patients had undergone a tumor staging change. Future studies are required to determine whether these differences result in an effect on patient outcomes, including recurrence and survival rates.

References

1. Patel SG, Shah JP. TNM staging of cancers of the head and neck: striving for uniformity among diversity. *CA: a cancer journal for clinicians* 2005; 55:242-258.
2. Patel NN, Faris C, Upile T. Getting the basics right-staging in head and neck cancer. *Head & neck oncology* 2009; 1:16.
3. Friedland PL, Bozic B, Dewar J, Kuan R, Meyer C, Phillips M. Impact of multidisciplinary team management in head and neck cancer patients. *British journal of cancer* 2011; 104:1246-1248.
4. Edge SB, Compton CC. The American Joint Committee on Cancer: the 7th edition of the AJCC cancer staging manual and the future of TNM. *Annals of surgical oncology* 2010; 17:1471-1474.
5. Lassig AA, Joseph AM, Lindgren BRet al. The effect of treating institution on outcomes in head and neck cancer. *Otolaryngology--head and neck surgery : official journal of American Academy of Otolaryngology-Head and Neck Surgery* 2012; 147:1083-1092.
6. Sdvizhkov AM, Kozhanov AG, Shatskaia N, Iadykov OA. [Delayed results of the treatment of patients with laryngeal cancer in Moscow]. *Vestnik otorinolaringologii* 2009:20-22.
7. David JM, Ho AS, Luu M, Yoshida EJ, Kim S, Mita AC, Scher KS, Shiao SL, Tighiouart M, Zumsteg ZS. Treatment at high-volume facilities and academic centers is independently associated with improved survival in patients with locally advanced head and neck cancer. *Cancer* 2017; 123:3933-3942.
8. Chen AY, Fedewa S, Pavluck A, Ward EM. Improved survival is associated with treatment at high-volume teaching facilities for patients with advanced stage laryngeal cancer. *Cancer* 2010; 116:4744-4752.
9. Karakohyun-Celik O AM, Olmezoglu A, Buyukpolat MY, Ozkok S et al. Practice patterns for oropharyngeal cancer in radiation oncology centers of Turkey. *Tumori* 2014:284-288.

0. Sharma A, Schwartz SM, Mendez E. Hospital volume is associated with survival but not multimodality therapy in Medicare patients with advanced head and neck cancer. *Cancer* 2013; 119:1845-1852.
1. Braunius WW, van Gils CH, Rosenberg AJ, Hordijk GJ, Moons KG. Observing stage-shifts in head and neck squamous cell carcinoma from initial clinical outpatient staging to definite clinical tumour board staging using radiological and endoscopical investigations: will less do? *Clinical otolaryngology : official journal of ENT-UK ; official journal of Netherlands Society for Oto-Rhino-Laryngology & Cervico-Facial Surgery* 2011; 36:352-360.
2. Broumand V, Lozano TE, Gomez JA. Evaluation and staging of oral cancer. *Oral and maxillofacial surgery clinics of North America* 2006; 18:435-444.
3. Lubek JE, Clayman L. An update on squamous carcinoma of the oral cavity, oropharynx, and maxillary sinus. *Oral and maxillofacial surgery clinics of North America* 2012; 24:307-316, x.
4. Lewis CM, Hessel AC, Roberts DB et al. Prereferral head and neck cancer treatment: compliance with national comprehensive cancer network treatment guidelines. *Archives of otolaryngology--head & neck surgery* 2010; 136:1205-1211.
5. Wheless SA, McKinney KA, Zanation AM. A prospective study of the clinical impact of a multidisciplinary head and neck tumor board. *Otolaryngol Head Neck Surg* 2010; 143:650-654.
6. Kesson EM, Allardice GM, George WD, et al. Effects of multidisciplinary team working on breast cancer survival: retrospective, comparative, interventional cohort study of 13 722 women. *BMJ* 2012; 344:e2718.
7. Kurpad R, Kim W, Rathmell WK, et al. A multidisciplinary approach to the management of urologic malignancies: does it influence diagnostic and treatment decisions? *Urol Oncol* 2011; 29:378-82.

8. van Hagen P, Spaander MC, van der Gaast A, et al. Impact of a multidisciplinary tumour board meeting for upper-GI malignancies on clinical decision making: a prospective cohort study. *Int J Clin Oncol* 2013; 18:214–9.
9. Oxenberg J, Papenfuss W, Esemuede I, et al. Multidisciplinary cancer conferences for gastrointestinal malignancies result in measureable treatment changes: a prospective study of 149 consecutive patients. *Ann Surg Oncol* 2015; 22:1533–9.
0. Greer HO, Frederick PJ, Falls NM, et al. Impact of a weekly multidisciplinary tumor board conference on the management of women with gynecologic malignancies. *Int J Gynecol Cancer* 2010; 20:1321–5.
1. Pillay B, Wootten AC, Crowe H, et al. The impact of multidisciplinary team meetings on patient assessment, management and outcomes in oncology settings: a systematic review of the literature. *Cancer Treat Rev* 2016; 42:56–72.
2. Huang SH, O'Sullivan B. Overview of the 8th Edition TNM Classification for Head and Neck Cancer. *Curr Treat Options Oncol* 2017; 18:40.
3. Loevner LA, Sonners AI, Schulman BJet al. Reinterpretation of cross-sectional images in patients with head and neck cancer in the setting of a multidisciplinary cancer center. *AJNR American journal of neuroradiology* 2002; 23:1622-1626.
4. Lysack JT, Hoy M, Hudon MEet al. Impact of neuroradiologist second opinion on staging and management of head and neck cancer. *Journal of otolaryngology - head & neck surgery = Le Journal d'oto-rhino-laryngologie et de chirurgie cervico-faciale* 2013; 42:39.

Table 1. Patient Demographics

Patient Characteristics	Percent of total (N = 159)
Sex	
Male	77
Female	23
Age (Years)	60
Race	
European American/White	91
African American/Black	6
Asian	1
American Indian/Eskimo/Aleutian	2
Other	1
Baseline tobacco status	
Never smoker	25
Current in past 12 mo	47
Former smoker >12mo	28
Baseline alcohol status	
Never drinker	8
Current drinker	69
Former drinker >12mo	23
BMI Category	
Underweight	7

Normal	40	328
Overweight	32	329
Obese	21	330
Recurrence		
Alive, no recurrence	77	
Recurred or persistence	23	
Disease Persistence		
No disease present after treatment	88	
Disease present after treatment completed or palliative at baseline	12	
Education Level		
	(N = 121)	
Less than High School	6	
High School or GED	30	
Some College	37	
4 year degree or greater	27	
Marital Status		
	(N = 155)	
Married	67	
Widowed	10	
Separated or divorced	8	
Never married	14	
Median Household Income (\$)		
	48,202.00	
Average Wait Time		
	14.7 days	
	(Range 0-163 days)	

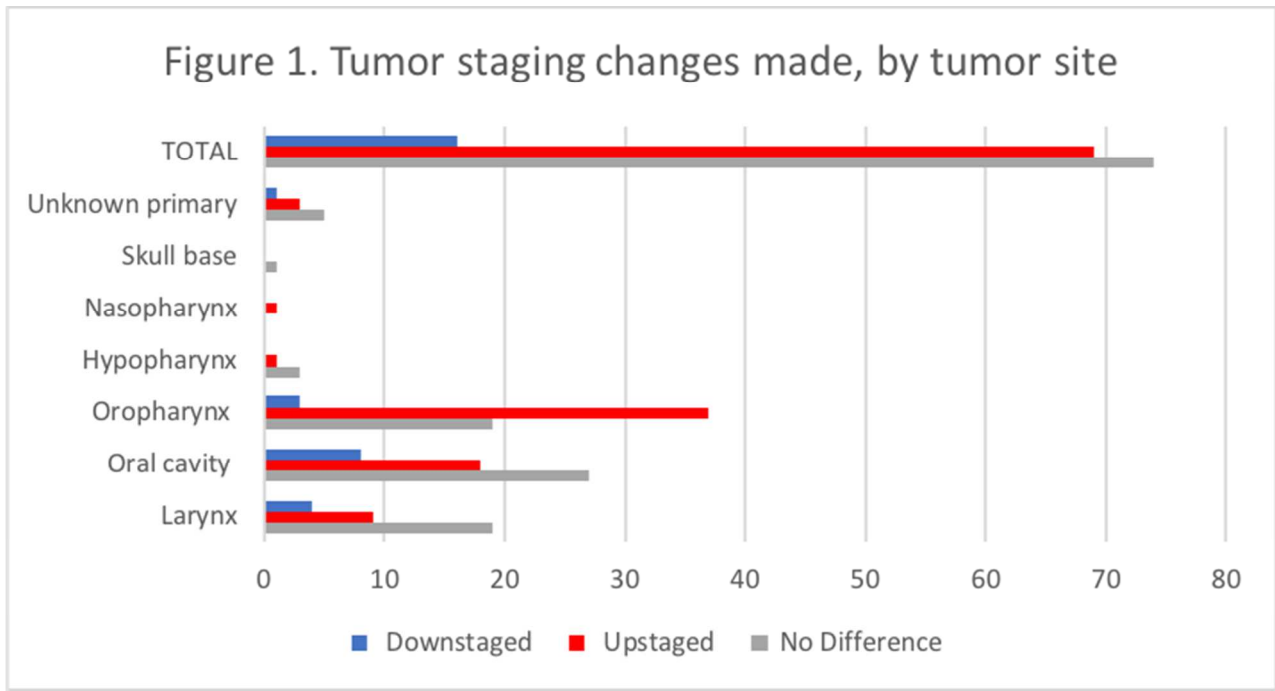
Table 2. Patient tumor sites and stages determined by tertiary care center

Tumor Site	Stage 1	Stage 2	Stage 3	Stage 4	Total
Larynx	10	4	4	14	32
Oral cavity	7	11	8	27	53
Oropharynx	2	0	8	49	59
Hypopharynx	0	0	1	3	4
Nasopharynx	0	0	0	1	1
Skull base	0	0	0	1	1
Unknown primary	0	0	1	8	9
TOTAL	19	15	22	103	159

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Table 3. Tumor staging changes made, by tumor site

Tumor Site	No Difference	Stage Difference		Percent Staged Differently
		Upstaged	Downstaged	
Larynx	19	9	4	41
Oral cavity	27	18	8	49
Oropharynx	19	37	3	68
Hypopharynx	3	1	0	25
Nasopharynx	0	1	0	100
Skull base	1	0	0	0
Unknown primary	5	3	1	44
TOTAL	74	69	16	53



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Table 4. Patient characteristics of patients with and without tumor stage change

Patient Characteristics	No Stage Difference	Stage Difference			P-value*
		Upstaged	Downstaged	Total	
Sex					0.109
Male	53	58	11	69	
Female	21	11	5	16	
Race					0.42
European American/White	65	65	15	80	
African American/Black	6	3	0	3	
Asian	1	0	0	0	
American Indian/Eskimo/Aleutian	1	1	1	2	
Other	1	0	0	0	
Baseline tobacco status					0.20
Never smoker	14	22	4	26	
Current in past 12 mo	39	27	8	35	
Former smoker >12mo	21	20	4	24	
Baseline alcohol status					0.97
Never drinker	5	6	1	7	
Current drinker	52	45	13	58	
Former drinker >12mo	17	18	2	20	
BMI Category					0.61
Underweight	7	4	0	4	
Normal	27	26	10	36	

Overweight	25	23	3	26	
Obese	15	16	3	19	
Recurrence					0.54
Alive, no recurrence	57	53	12	65	
Recurred or persistence	17	16	4	20	
Disease Persistence					0.57
No disease present after treatment	65	62	13	75	
Disease present after treatment completed or palliative at baseline	9	7	3	10	
Education Level					0.93
Less than High School	3	2	2	4	
High School or GED	19	11	6	17	
Some College	21	21	3	24	
4 year degree or greater	17	13	3	16	
Marital Status					0.39
Married	51	46	7	53	
Widowed	5	7	4	11	
Separated or divorced	8	4	1	5	
Never married	9	10	3	13	

*Fisher exact test was conducted for each category comparing the number of patients with no stage difference to the total number of patients with a stage difference, either upstaged or downstaged