Clinical Predictors of Treatment and Survival Outcomes in Distant Metastatic Head and Neck Cancer: A Multicenter Review

Craig A Bollig, MD[1]; Chris I Newberry, MD[2]; Tabitha L I Galloway, MD[3]; Robert P Zitsch, III, MD[3]; Elyse K Hanly, MD, PhD[4]; Vivian I Zhu, MD[4]; Nitin Pagedar, MD, MPH[4]; Rohit Nallani, MD[5]; Andres Bur, MD[5]; William C Spanos, MD[6]; Jeffrey B Jorgensen, MD[7]; [1]Rutgers Robert Wood Johnson Medical School; [2]Washington University in St. Louis; [3]University of Missouri; [4]University of Iowa; [5]University of Kansas; [6]Sanford Cancer Center; [7]University of Louisville

Introduction

Distant metastases (DM) may develop in approximately 10-20% of patients with squamous cell carcinoma of the head and neck (HNC). They are associated with a poor prognosis and further treatment is usually palliative or supportive. Existing studies in HNC patients with DM are generally limited by small sample size, particularly in the less commonly affected metastatic sites. As a result, there is relatively limited information regarding potential differences in survival and treatment outcomes among sites of DM in patients with HNC. Additionally, there is limited information on clinical factors associated with systemic and metastasis directed treatment (MDT) in this population.

Our objectives with this study were to:

1) Investigate the relationship between clinicopathologic factors including site and pattern of DM and overall survival (OS) in a multi-institutional cohort of HNC patients with DM.
2) 2) Identify clinical variables associated with administration of MDT and systemic treatment.

Methods

After IRB approval was obtained from all participating institutions, a retrospective analysis of 269 patients with distant metastatic HNC treated at 4 academic centers in the Midwest HNC Consortium between 2000 and 2015 was performed.

Baseline covariates were compared between treatment groups using ANOVA or chi-squared test for continuous or categorical values, respectively. OS was analyzed based on patient demographics and clinical factors using Kaplan-Meier and Cox proportional hazards models. Clinical factors associated with no treatment, as well as administration of MDT and systemic treatment were determined using logistic regression.

SPSS v26 software was used for data analysis (SPSS Inc, an IBM Company, Chicago, Illinois).

Results

Table 1. Patient Characteristics

	No Tx (n= 74)	Systemic Only (n= 74)	MDT +/- Systemic (n= 121)	p value
Age, mean (SD)	62.6 (11.8) years	58.6 (10.0) years	58.9 (10.7) years	0.039
Gender				0.072
Male	54 (73.0%)	65 (87.8%)	98 (81.0%)	
Race				0.973
White	64 (86.5%)	62 (83.8%)	102 (84.3%)	
Primary Site				0.248
Oral Cavity	16 (21.6%)	12 (16.2%)	21 (17.4%)	
Oropharynx	20 (27.0%)	23 (31.1%)	51 (42.1%)	
Larynx	23 (31.1%)	22 (29.7%)	27 (22.3%)	
Hypopharynx	12 (16.2%)	11 (14.9%)	10 (8.3%)	
Nasopharynx	1 (1.4%)	5 (6.8%)	7 (5.8%)	
Sinonasal	2 (2.7%)	1 (1.4%)	5 (4.1%)	
Initial T Stage				0.792
T1/2	23 (31.1%)	26 (35.1%)	36 (29.8%)	
T3/4	49 (66.2%)	44 (59.5%)	78 (64.5%)	
Tx	2 (2.7%)	4 (5.4%)	7 (5.8%)	
Initial N Stage				0.590
N0	7 (9.5%)	4 (5.4%)	11 (9.1%)	
N+	67 (90.5%)	70 (94.6%)	110 (90.9%)	
Previous Treatment				
None Recorded	21 (28.4%)	6 (8.1%)	39 (32.2%)	<0.001
Surgery	36 (48.6%)	40 (54.1%)	48 (39.7%)	0.129
Radiation Therapy	46 (62.2%)	65 (87.8%)	81 (66.9%)	0.001
Chemo	31 (41.9%)	51 (68.9%)	61 (50.4%)	0.003

Table 2. Median Overall Survival by Metastatic Site, Pattern, and Treatment Modality

	No Treatment OS [95% CI]	Systemic Therapy Only OS [95% CI]	MDT + Systemic Therapy OS [95% CI]
All Patients (n=269)	2.0 [1.2- 2.8] Months	12.0 [9.5- 14.5] Months	12.0 [10.2- 13.8] Months
Solitary Metastasis (n= 53)	1.0 [0- 2.0] Months	11.0 [8.2- 13.8] Months	19.0 [12.2- 25.8] Months
Polymetastases (n= 216)	2.0 [0.8- 3.2] Months	12.0 [7.7- 16.3] Months	11.0 [8.0- 14.0] Months
Single Organ (n=158)	3.0 [1.6- 4.4] Months	12.0 [9.3- 14.7] Months	15.0 [10.9- 19.1] Months
Multi Organ (n=111)	1.0 [0.2- 1.8] Months	10.0 [3.5- 16.5] Months	11.0 [7.0- 15.0] Months
Lung (n= 207)	2.0 [0.7- 3.3] Months	12.0 [9.5- 14.5] Months	12.0 [10.2- 13.8] Months
Mediastinal Lymph Node (n= 51)	2.0 [0.7- 3.3] Months	12.0 [9.4- 14.6] Months	7.0 [0- 19.5] Months
Bone (n= 87)	1.0 [0- 3.6] Months	10.0 [6.1- 13.9] Months	8.0 [5.2- 10.8] Months
Liver (n= 40)	2.0 [1.2-2.8] Months	12.0 [9.5- 14.5] Months	12.0 [10.2- 13.8] Months
Brain (n= 17)	6.0 Months^	6.0 Months^	21.0 [11.8- 30.2] Months

^ denotes insufficient sample size

Table 3. Clinical Factors Associated with Overall Survival, Multivariable Analyses

Primary Site	Hazard Ratio	95% Confidence Interval
Oropharynx	Ref.	
Oral Cavity	1.53	[1.07- 2.18]
Larynx	1.33	[0.97- 1.84]
Hypopharynx	1.05	[0.70- 1.59]
Nasopharynx	0.93	[0.50- 1.72]
Sinonasal	2.77	[1.33- 5.78]
Metastatic Site		
Bone	1.71	[1.30- 2.26]
Treatment		
None	Ref.	
Systemic Therapy Only	0.31	[0.22- 0.44]
MDT +/- Systemic Therapy	0.22	[0.16- 0.31]

Table 5. Clinical Factors Associated with No Treatment, Multivariate Analysis

Institution	Odds Ratio	95% Confidence Interval
A	Ref.	
B	0.39	[0.17- 0.88]
C	0.48	[0.24- 0.93]
D	0.23	[0.06- 0.89]
Age, mean (SD)	1.03	[1.01- 1.06]

Table 5. Clinical Factors Associated with MDT, Multivariate Analysis

	Odds Ratio	95% Confidence Interval
Primary Site		
Oropharynx	1.67	[1.01- 2.78]
Non-Oropharynx	Ref.	
Metastatic Site		
Brain Metastasis	5.87	[1.63- 21.10]

Table 5. Clinical Factors Associated with Systemic Treatment, Multivariate Analysis

Institution	Odds Ratio	95% Confidence Interval
A	Ref.	
B	2.39	[1.10- 5.19]
C	1.87	[0.97- 3.60]
D	0.23	[0.06- 0.89]
Age, mean (SD)	0.97	[0.94- 0.99]
Gender		
Male	Ref.	
Female	0.48	[0.25- 0.93]

Conclusion

Our large multicenter review suggests that treating institution, site of metastasis (brain), primary site (oropharynx), and gender may be associated with receipt of treatment in patients with distant metastatic head and neck cancer.

References

1. Garavello W, Ciardo A, Spreafico R, Gaini RM. Risk Factors for Distant Metastases in Head and Neck Squamous Cell Carcinoma. *Arch Otolaryngol Head Neck Surg.* 2006;132(7):762–766.
2. De Bree, R., E. E. Deurloo, G. B. Snow, and C. R. Leemans. 2000. Screening for distant metastases in patients with head and neck cancer. Laryngoscope 110:397–401.
3. Dennington, M. L., D. R. Carter, and A. D. Meyers. 1980. Distant metastases in head and neck epidermoid carcinoma. Laryngoscope 90:196–201.
4. Black, R. J., J. L. Gluckman, and D. A. Shumnick. 1984. Screening for distant metastases in head and neck cancer patients. Aust. N. Z. J. Surg. 54:527–530.
5. Haigentz M Jr, Harti DM, Silver CE, et al. Distant metastases from head and neck squamous cell carcinoma. Part III. Treatment. *Oral Oncol.* 2012;48(9):787-793
6. Ferlito A, Shaha AR, Silver CE, Rinaldo A, Mondin V. Incidence and sites of distant metastases from head and neck cancer. *ORL J Otorhinolaryngol Relat Spec.* 2001;63(4):202-207.
7. Takes RP, Rinaldo A, Silver CE, et al. Distant metastases from head and neck squamous cell carcinoma. Part I. Basic aspects. *Oral Oncol.* 2012;48(9):775-779.